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Editors J. R. BELCHER *and* J. SMART

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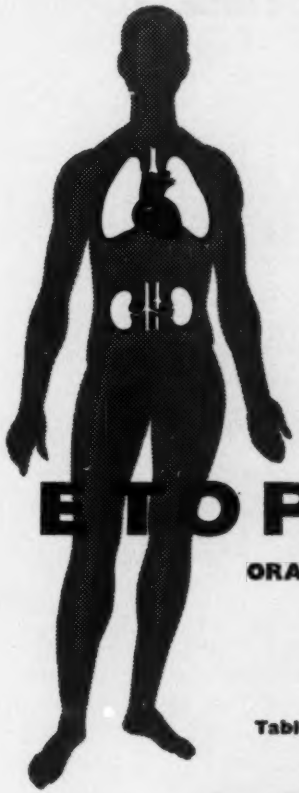

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Brit. J. Dis. Chest (1960) **54**, 297.

THE UNEMPLOYMENT PROBLEMS ASSOCIATED WITH CHRONIC BRONCHITIS IN EAST LONDON

By Maxwell Caplin and C. P. Silver

From the Tuberculosis Dispensary, London Chest Hospital

This survey of the employment history of 83 cases of chronic bronchitis living in the East London borough of Hackney has three purposes. The first is to analyse the problems facing unemployed bronchitics. The second is to draw attention to the present arrangements for helping such cases to find suitable employment. The third is to put forward suggestions for improving these arrangements in the future.

The chronic bronchitic suffers from two disabilities which may make it difficult for him to retain his usual employment or find new employment. These are increasing shortness of breath on exertion and lung infections which force him to be away from work for a varying period. As the condition develops the bronchitic subject finds difficulty in travelling to work, keeping up with others at his work, and in working in a dusty or polluted atmosphere. In the more advanced stages he may become so crippled by his shortness of breath as to be as handicapped as the paraplegic patient, and to constitute an equally serious employment problem.

The Disabled Persons (Employment) Acts, 1944 and 1958, were designed to assist such cases. A disabled person was defined as one who on account of injury, disease or congenital deformity is substantially handicapped in getting or keeping suitable employment or work. A Register of disabled persons is kept at every employment exchange and special efforts are made to place them suitably. How do these measures affect the bronchitic? What kind of bronchitic is referred for registration, and if registered what help does he receive? These are some of the questions that this survey attempts to answer.

The Borough of Hackney

The Borough of Hackney lies in the north-eastern part of the County of London and has a population of approximately 170,000 (1951 census), of whom 57,000 are occupied males over the age of 15. Its southern part is largely industrial, and clothing and furniture manufacturing are important local industries. The Hackney Employment Exchange serves both the boroughs of Hackney and Stoke Newington, having a total population of approximately 214,000, and the total number of Registered Disabled Males in April 1958 was 2,614, of whom 197 or 7·6 per cent. were suffering from bronchiectasis, bronchitis or emphysema. The comparable percentage for the whole country was 6·4 per cent.

(*Received for publication, June 15, 1960.*)

The Cases

There were 83 cases, all of whom had chronic cough, sputum and shortness of breath. None had evidence of underlying disease such as active tuberculosis or pneumoconiosis. They can be regarded as cases of chronic bronchitis already suffering from complications and, therefore, in the later stages of the disease (Fletcher, Elmes, Fairbairn and Wood, 1959). The survey was restricted to males between the ages of 40 and 64 living in Hackney. Thirty-four were hospital out-patients, 26 were attending their general practitioners, and 23 were in-patients in a local general hospital. All were questioned concerning their occupations, their periods of unemployment, whether registered as disabled and the results of registration, and all names were checked at the local employment exchange for details regarding registration to be verified. The cases fell into three groups, those who were never registered as disabled (Unregistered Cases), those who were on the Register at the time of the survey (Registered Cases, still on Register), and those who were registered in the past, but had been removed from the Register for various reasons (Registered Cases, removed from Register).

Age Distribution

Approximately one-third of the cases were under 55 years of age.

Table 1.—Age Distribution and Registration

Age group	*All cases*	*Unregistered cases*	*Registered cases*		
			All	*Still on*	*Removed*
40-44	6	3	3	1	2
45-49	4	3	1	1	0
50-54	19	11	8	4	4
55-59	25	19	6	4	2
60-64	29	22	7	4	3
Totals	83	58	25	14	11

Fifty-eight cases (70 per cent.) had never been registered as disabled. Twenty-five (30 per cent.) had been registered at some time, and of these nearly half had been removed from the Register, leaving 14 (17 per cent.) who were on the Register at the time of the survey. Registration was more common amongst the younger bronchitics. Of those under 55 years of age, 12 (41 per cent.) had been registered; over 55, 13 (21 per cent.) had been registered.

Main Occupation and Social Class

For the purpose of this survey the main occupation was the one engaged in for the longest period. In practically all cases this was over fifteen years and covered the early stages of bronchitis. The occupations have been classified according to the Occupation Tables, Census 1951, England and Wales, and are shown in Table 2.

TABLE 2.—OCCUPATION AND REGISTRATION

	Transport workers	*Textile goods makers*	*Engineering workers*	*Woodworkers*	*Unskilled workers (Not elsewhere specified)*	*Building workers*	*Others*
Unregistered cases	15	6	5	9	4	4	15
Registered cases	3	3	2	3	7	4	3
All cases	18	9	7	12	11	8	18

The commonest occupational groups were, in order, transport workers, woodworkers, and unskilled workers. The last group consists of unskilled workers who cannot be classified under other occupational headings. It will be seen that 3 of the 18 transport workers were registered, compared with 7 of the 11 unskilled workers. This suggests that the bronchitic unskilled worker has greater difficulty in finding work without assistance than the bronchitic transport worker, and is therefore more likely to be referred for registration.

Social class is a more effective method of gauging skill for our purpose than occupational grouping, because each occupational group is made up of workers of varying degrees of skill. The five social classes are arrived at by classifying individual jobs into broad categories of approximately the same level of skill and general standing. Social Class I is made up of professional and similar occupations, Class II of those in occupations intermediate between professional and skilled, Class III of skilled, Class IV of partly skilled, and Class V of unskilled workers.

Among the bronchitics there was one in Class II. There were 44 in Class III and 38 in Classes IV and V. In Class III there were 17 under 55 years of age and 27 over, and in Classes IV and V, 11 under 55 and 27 over, *i.e.* there were relatively more of the older bronchitics in Classes IV and V.

Registration was more frequent in those lacking a skill. Thus in Classes IV and V, 45 per cent. (17 cases) were registered, compared with 18 per cent. (8 cases) in Class III. It will be recalled that younger bronchitics were more likely to be registered (Table 1). Since registration was more common in Classes IV and V, and these classes had fewer young bronchitics, it follows that social class is a factor influencing registration and is independent of age.

In Hackney 13 per cent. of the general population are in Classes I and II, 61 per cent. in Class III and 26 per cent. in Classes IV and V. Amongst the bronchitics 53 per cent. were in Class III and 46 per cent. in Classes IV and V. This increased proportion of Classes IV and V may be explained by the fact that two-thirds of these cases were attending an out-patient department or were patients in a local general hospital; or it may be explained by a greater incidence of bronchitis amongst the lower social classes. The latter explanation would be in keeping with the findings in the Newcastle Survey (Ogilvie and

Newell, 1957), and the Registrar-General's figures for mortality from bronchitis which show a five-fold mortality in Class V as compared with Class I.

Time Lost from Work on Account of Bronchitis

Time lost from work may be due either to sickness or to unemployment. When eliciting a retrospective history from bronchitics it is often difficult to determine whether loss of time is due to sickness or to unemployment, as there is a tendency for cases to continue to draw sickness benefit though fit for some form of work, because such work is not available. However, time lost calculated in this way must give a good guide to the severity of the bronchitic's disablement in relation to his particular occupation. For example, though equally breathless, the clerk working under good conditions near his home will return to work earlier than the builder's labourer whose work may be far from his home.

Table 3.—Average Time in Months Lost on Account of Bronchitis, during the Past Year, and during the Past Three Years, related to Age and Registration

	Age group	*All cases*	*Unregistered cases*	*Registered cases*	
				Still on	*Removed*
Time lost in past year	Under 55	5·1	4·2	5·8	7·0
	Over 55	7·0	6·2	7·9	12·0
	All ages	6·3	5·6	7·0	9·3
Time lost in past three years	Under 55	11·9	8·7	13·5	19·7
	Over 55	16·2	13·6	17·3	36·0
	All ages	14·7	12·2	15·6	27·1

Table 3 shows that the bronchitics lost on an average approximately six months in the past year and fifteen months in the past three years. Time lost increased with age, and Registered cases lost more time than Unregistered. The greatest loss of time occurred among bronchitics removed from the Register. Those over 55 in this group lost the whole period.

When loss of time is considered in relation to social class it is those who lack a skill who come off worst. During the past three years the average time lost by those in Classes IV and V was 18·9 months, compared with 11·2 months lost by those in Class III.

Table 4 shows that a serious loss of time, *i.e.* one year during the past three years, was lost by nearly half the bronchitics. Again the numbers increase with age and also with registration.

It is reasonable to assume that when any bronchitic has lost a year from work during the past three years his employment difficulties need investigating to see whether a more suitable job could be found. It is also reasonable to assume that such bronchitics are handicapped within the meaning of the Disabled Persons (Employment) Act, and should therefore be offered registration. Yet 22 Unregistered cases (38 per cent.) had lost such time.

TABLE 4.—NUMBER OF CASES WHO LOST ONE YEAR OR MORE DURING THE PAST THREE YEARS, RELATED TO AGE
(The total number of cases in each group shown in brackets)

Age group	*All cases*	*Unregistered cases*	*Registered cases*		
			All	*Still on*	*Removed*
Under 55	9 (29)	3 (17)	6 (12)	3 (6)	3 (6)
Over 55	29 (54)	19 (41)	10 (13)	5 (8)	5 (5)
All ages	38 (83)	22 (58)	16 (25)	8 (14)	8 (11)

FITNESS FOR WORK, AND PRESENT EMPLOYMENT

Each bronchitic was graded by his doctor into one of three broad categories: first, suitable for full-time light work in ordinary industry; secondly, requiring work under sheltered conditions (sheltered workshop or work at home); and finally, unemployable on account of bronchitis. The cases were asked at the same time whether they were employed at present or whether they had a job to return to when well again.

TABLE 5.—FITNESS FOR WORK RELATED TO AGE
(Number of cases who had no job to return to in brackets)

	Under 55	*Over 55*	*All cases*
Light work ..	17 (2)	24 (5)	41 (7)
Sheltered work ..	10 (6)	22 (17)	32 (23)
Unemployable ..	2 (2)	8 (8)	10 (10)
All cases	29 (10)	54 (30)	83 (40)

Table 5 shows that 41 (49 per cent.) required full-time light work, 32 (39 per cent.) required sheltered work, and 10 (12 per cent.) were considered unemployable. The proportion who required sheltered work or were unemployable increased with age.

The proportion of cases who had no job to return to also increased with age. Of all bronchitics 40 (48 per cent.) had no job to return to. Of those suitable for full-time light work 7 (17 per cent.), and of those requiring sheltered work 23 (72 per cent.), had no job to return to.

Table 6 shows that 25 (43 per cent.) of the Unregistered cases were unfit for full-time light work, whereas the comparable figure for Registered cases was 17 (68 per cent.). Since medical grading of fitness for work runs parallel with severity of bronchitis, these figures would suggest that the Registered cases include a higher proportion of the more severe bronchitics. However, not all the Registered Cases were severe. Eight cases (32 per cent.) were fit for full-

TABLE 6.—FITNESS FOR WORK RELATED TO REGISTRATION

	All cases	*Unregistered cases*	*Registered cases*		
			All	*Still on*	*Removed*
Light work ..	41	33	8	4	4
Sheltered work ..	32	18	14	8	6
Unemployable ..	10	7	3	2	1
All cases	83	58	25	14	11

time light work. On the other hand, among Unregistered cases there were 18 requiring sheltered work; indeed there were 7 who had reached the stage of unemployability but yet had never been registered.

Of the 18 Unregistered cases requiring sheltered work, 13 had no job to return to, as had 10 of the 14 Registered cases.

CASES STILL ON THE REGISTER

The average age on registration for the 14 cases in this group was 50 years, and the length of time since registration varied from five months to twelve years. The average loss of time during the past year for 9 cases who had been registered for more than a year was six months. The cases had been referred for registration by hospitals, general practitioners, and at the suggestion of their employers. For example, a bus conductor registered when he became a lost property attendant, while a Hoffman presser remained at the same job but registered because his firm was anxious that he "should have a green card." Frequently a variety of jobs was held, interspersed with periods of sickness and unemployment. Some jobs were found with the help of the employment exchange and some by the men themselves. Five cases continued to work for their original employer, and 4 of these had a job to return to. Of 9 cases who had changed employment after registration only 3 had a job to return to.

CASES REMOVED FROM THE REGISTER

The date of registration of the 11 cases in this group could be traced only in 7 cases. The average age on registration of these was 45 years, and the length of time on the Register varied from one to eleven years.

Eight cases failed to renew their registration. Two of these had lost less than a year from work during the past three years and were in suitable jobs. The remaining 6 cases had been away from work for a long period during the past three years; 4 had lost the whole period.

Three cases had their names removed from the Register by Disablement Advisory Committee Panels, one because registration was considered unnecessary on review (he had lost five months from work during the past three years) and two because they were considered unemployable.

Discussion

The bronchitic's unemployment problems can be discussed under three headings; the bronchitic himself, his doctor, and the working of the Disabled Persons (Employment) Act.

The Bronchitic Case

Once bronchitis is established the progress is usually one of deterioration. The rate of progress is variable, but the effect on his employment follows a fairly general pattern. Since the first hour or two after waking in the morning is usually the worst time for the bronchitic he gets up earlier in order to allow himself time to " clear his chest." He also starts out earlier for work because his journey now takes him longer. Sooner or later he begins to worry about losing his job because he finds he is unable to keep up the pace at work, and because of periods of sickness and his increasing age.

In large industries a more suitable job may be made available for him, particularly if he is a skilled worker with a long record of service. In industries where the gang or team system operates, *e.g.* dock labourers, the rest of the group may for a time shield him from the heavier work. But in the smaller industries his employer may dismiss him. At this stage he is a middle-aged or elderly man able only to do work which is light, non-dusty and near his home. He may try job after job initially in the same occupation, and subsequently will attempt to find work in a different occupation. In this survey 37 per cent. of the cases changed their main occupation, and 17 per cent. had more than one such change. Some of this work may be quite unsuitable from the point of view of bronchitis, and as his condition progresses he is regarded and regards himself as unemployable.

The Doctor

Since unsuitable work may aggravate bronchitis it is reasonable to assume that the provision of suitable work may slow the progress of the disease and therefore should be regarded as an important part of medical treatment. Yet it is clear that only a minority of bronchitics who are handicapped and who require help in finding employment are referred by their doctors for registration. Of 32 considered suitable for sheltered work, only 8 were registered; of 38 away from work for a year or more in the past three years, 8 were registered; and of 40 who had no job to return to, 7 were registered.

Some doctors may not be fully aware of the facilities available, but others regard registration as a waste of time. If registration proved effective the doctor would be aware of it, and he would have no hesitation in referring disabled bronchitics.

The Working of the Disabled Persons (Employment) Act

The Disablement Resettlement Officers (D.R.O.s) in this part of London work energetically in an attempt to place the unemployed registered bronchitic in the right type of employment, but such employment is rarely available.

It has been shown in the previous sections that two thirds of the bronchitics were over 55 years of age, nearly half lacked a skilled occupation, nearly half lost a year from work during the past 3 years, only half were fit for full-time light work, and more than a third required some form of sheltered work. Finding suitable work in these circumstances presents a formidable task for the D.R.O.

A recent analysis showed that there were 49,000 registered disabled persons suffering from chronic bronchitis and bronchiectasis, and of these some 3,700 were unemployed, *i.e.* approximately 8 per cent. Many, however, were receiving Sickness Benefit and were therefore not known to the employment exchanges. In this country chronic bronchitis is the commonest cause of loss of time from work through sickness, and cases frequently continue to receive Sickness Benefit though fit for some form of work, because in the doctor's mind the distinction between fitness and unfitness for work depends on the likelihood of a suitable job being available.

The ideal employment for the bronchitic should combine the following:

1. A non-dusty atmosphere.
2. Work which he can do at his own pace.
3. Little or no travelling.
4. A wage that exceeds his income from Sickness Benefit and National Assistance.

Under the provisions of the Act the D.R.O. has various means of helping unemployed registered disabled persons. The chronic bronchitic, however, because of his particular needs is not adequately catered for by the present provisions. These are:

1. *Industrial Rehabilitation and Vocational Training Courses.* Industrial Rehabilitation courses last about eight weeks and are designed to improve physical fitness. Vocational training lasts six months or more and gives training in a variety of occupations. Bronchitics are generally excluded from both types of course on account of age and the considerable travelling that is frequently involved.

2. *The Quota Scheme.* Section 9 of the Act imposes a duty on every employer of twenty or more persons to give employment to a quota of registered disabled persons. However, sometimes employers fulfil their obligations by seeking out persons with minor disabilities on their own staffs whose employment is not threatened and so avoid taking on unemployed registered disabled persons. This is one reason why the D.R.O. does not have sufficient vacancies for those who are handicapped in getting suitable employment.

3. *Designated Employment.* So far only two employments have been reserved for disabled persons: car-park attendant and passenger electric lift attendant. The first is unsuitable for the chronic bronchitic, and there are few vacancies for the second.

4. *Employment under Sheltered Conditions.* Sheltered work is provided by Remploy Ltd., local authorities and voluntary organisations. Remploy is the

largest employer, and the type of work provided approaches the ideal for the bronchitic in that it is light and he is allowed to do it at his own pace. However, there are only ninety factories in the country and therefore travelling is a serious problem. Remploy also employ homeworkers and this scheme comes closest to the ideal solution to the elderly bronchitics' problems. Their numbers are small and fell from 121 at the end of 1957 to 95 at the end of 1958. The fall was ascribed to lack of suitable work (Report on Resettlement of Disabled Persons, 1958).

In 1958 Remploy employed 6,200 workers with an operating loss of £2,800,000, *i.e.* £450 a man per annum. The average wage was £7 9s. 5d. *i.e.* £389 per annum. The present waiting list for all disabled persons who could be employed by Remploy is 2,000. More Remploy factories are needed, but in view of the high capital cost of establishing them and the serious operating loss their growth must be slow. The number of homeworkers that Remploy is able to supply is at present a very small contribution to the solution of the problem.

The Future

Bronchitis is likely to remain a serious problem for many years to come. Indeed, because modern antibiotic treatment is tending to slow the progress and so prolong the course of the disease, many bronchitics will survive to become future unemployment problems. The Ministry of Labour and National Service in their most recent report on the Resettlement of Disabled Persons, 1958, mention as special problems the young disabled, blindness, tuberculosis, epilepsy, paraplegia and rheumatism. Bronchitis is not included. This may be because bronchitis is a progressive disease and because in this disease figures for unemployment are concealed in those for sickness. Yet if this sample of disabled bronchitics is at all typical of the rest of the country—and there is no reason to think that it is not—bronchitis produces a serious unemployment problem which can only be overcome by energetic methods.

To improve the employment prospects of bronchitics full use should be made of the powers conferred by the Act. It has been shown that the possession of a skilled occupation is likely to improve the subsequent employment course, and therefore the opportunity of acquiring a skill, particularly one not involving work in a dusty atmosphere, should be offered to all younger bronchitics. Special efforts should be made to train men older than those usually accepted. The quota system requires more strict enforcement; claims for registration should be carefully examined when firms fall below quota and refer their own employees.

In training of doctors greater emphasis should be laid on the part registration can play in the welfare of many with disabling disease. General practitioners should be kept in closer contact with local employment exchanges. Resettlement conferences at which patient, doctor and D.R.O. are present together should be more widely held. They allow regular review of the changing capabilities of the bronchitic.

Ultimately a considerable proportion of bronchitic cases will require some

form of sheltered work in the latter part of their working lives. With improving social conditions the employment of disabled persons becomes more practicable, but it is unrealistic to expect further huge subsidies for the extension of the Remploy scheme. Voluntary schemes for the employment of old people, such as Workrooms for the Elderly, East London, and Workshops for the Elderly, Hackney, have run successfully on a local basis for several years. Could not the same be done for the bronchitic, whose difficulties are not so different from those of the elderly?

A voluntary organisation should allow lower running costs and greater flexibility, while its local character would have the following advantages:

1. The benefit of local goodwill; the knowledge of local facilities and industrial conditions; acquaintance with the bronchitics themselves and their living conditions.
2. The size of the workshop would be related to the local needs, and the work done to the local industries.
3. Travelling, one of the major difficulties for bronchitics, would be much reduced, and in cases where it is necessary transport to and from work could more readily be arranged.
4. There could be local integration of homework and sheltered workshop. When the bronchitic is less well he could be transferred from workshop to homework. The homeworker in need of companionship and a change of surroundings could be brought for a period to the workshop.

For success two requirements must be met: a sufficient volume of the right sort of work and a financial subsidy. The right sort of work is to-day available in most areas, and with active support from local industries should be sufficient in volume for the needs of a local workshop. Where the volume is insufficient, government or local authority contracts or some statutory provision such as a quota on production in certain industries might be necessary.

Financial aid is essential to ensure that the worker's income exceeds that from Sickness Benefit and National Assistance. Without experiment it is impossible to know the size of this subsidy but, with a voluntary organisation, it should be less than that allowed to Remploy.

On these lines local workshops for bronchitics become a possibility. If successful their use could be extended to all disabled persons requiring sheltered work or work at home.

Summary

Eighty-three males with chronic bronchitis, aged 40 to 64, were questioned about their employment histories. Only 30 per cent. had been registered as Disabled Persons at any time and only 17 per cent. were on the Disabled Persons Register at the time of the survey. Registration was more common among younger bronchitics and among those in Social Classes IV and V (partly skilled and unskilled workers).

Advancing age and lack of skill were in every way unfavourable to the employment of the bronchitic.

Employment is discussed in relation to the bronchitic himself, his doctor and the statutory arrangements for helping him. Suggestions are made for improving the bronchitic's prospects of employment in the future.

We wish to thank the local medical practitioners and the staff of Hackney Hospital for their help; and Mr. G. R. Crosby, manager of Hackney Employment Exchange, and Mr. H. V. Manhood and Mr. F. W. T. Francis, Disablement Resettlement Officers, for their exceptional kindness and patience with our enquiries.

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A MAINTENANCE TRIAL OF COMBINED STEROID AND ANTIBIOTIC TREATMENT IN A SERIES OF ASTHMATICS WITH CHRONIC BRONCHITIS

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In a recent survey of an industrial city it was found that asthma was several times more prevalent among chronic bronchitics than among persons not so affected (Ogilvie and Newell, 1957).

Forty-two of 464 bronchitics were asthmatical as against 5 of 485 non-bronchitic persons (*i.e.* 9 per cent. against 1 per cent.). This figure of 1 per cent. is close to the national incidence of asthma (Williams, 1951). Considered in conjunction with the known difficulty which the asthmatic has in ridding himself of infection, this was interpreted as an indication that asthmatics are prone to develop chronic bronchitis: a conclusion generally accepted but partially masked by the lack of accepted criteria of diagnosis.

The patient who is increasingly disabled by continuous severe expiratory obstruction, associated with gross persistent wheezing and the clinical evidence of chronic bronchitis and emphysema, is far from uncommon in the medical out-patient department. Indeed if 9 per cent. of chronic bronchitics are asthmatical and if chronic bronchitis occurs in 30 per cent. of adult males in an industrial city, the problem is a large one requiring serious consideration.

This disorder is, in fact, an expensive one. Our patients' average earnings were approximately £11 10s. per week, and this value at least is lost to their employers, and thus to the national product when they are sick. Further, their average total income when sick is approximately £6 per week. This means, from the man's point of view, a loss of £5 10s. per week, and at the same time a charge to pension funds of £6 per week. Our objective in this study was to attempt to relate the cost of maintenance treatment to the gain achieved by enabling the patient to remain at work.

The association of chronic broncho-pulmonary infection with asthma has been observed in bronchiectasis. Strang (1956) carried out a follow-up of 209 children treated by Mason and his colleagues at Shotley Bridge between 1935 and 1948. Of these, 50 showed asthmatic symptoms which were severe in 8. Thirty-nine of these 50 were included in the 163 cases operated upon and accounted for 24 of 35 cases recorded as showing slight or no improvement, or as being worse, following operation.

May and Oswald (1956), Helm *et al.* (1956) and Edwards and Phear (1958) have claimed that recognisable improvement in a series of chronic bronchitic persons can be achieved by daily administration of Tetracycline over a prolonged period.

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It is felt that today little reference to the literature is necessary to support the view that steroids are effective in the treatment of bronchial asthma.

In the condition here referred to as persistent asthma with chronic bronchitis it appeared that both steroid and antibiotic therapy would be needed, both given more or less continuously over a period. Up to two years ago there were no reports of trials of this combined treatment, and it was decided to carry out a preliminary trial in a series of patients.

Criteria of Diagnosis

The patients were selected on clinical criteria, but were otherwise consecutive. They were not admitted in the phase of acute exacerbation, and treatment was not consistently continued after discharge. No control series was included, as it was felt that the natural history was sufficiently known, and the objective was the limited one of assessing the possibility of achieving improvement by this means. In fact, 86 cases out of 120 were dramatically improved for a short while (Ogilvie, 1958).

The 120 patients previously referred to were all subject to severe cough with phlegm and to chronic dyspnœa. All showed clinically respiratory obstruction with gross *persistent* wheezing. They gave a history of intermittent attacks of aggravated wheezing, or of exacerbation of symptoms less pronounced though usually more prolonged. Although other signs, and personal and familial "allergic" symptoms, were almost always present, only the above criteria were insisted on. The resulting response to treatment was held to justify this purely clinical approach.

In the present study the criteria of diagnosis were reconsidered but finally accepted again. A fairly constant observation was that, contrary to the rule in chronic bronchitis without asthma, cough and sputum became less obvious during exacerbations, and that the more severe the exacerbation the less the sputum.

It is clear from the work of Hume and Gandevia (1957), and of Thomson and Hugh-Jones (1958), that the asthmatic must be tested in a certain phase if a reliable response to an Isoprenaline aerosol is to be obtained and it is doubtful if even a positive response would be generally accepted as diagnostic. Robinson *et al.* (1958) reported that "practically all chronic bronchitics show an improvement in the forced expiratory volume after inhalation of powdered Isoprenaline." It is open to question if asthmatics were effectively excluded. But their criteria do not appear to be those which would readily include asthmatics. These were: "chronic productive cough, worse in winter, for two or more years, with dyspnœa on exertion and episodes of infected sputum." Morrow (1958) found that chronic asthmatics responded much better to treatment by Prednisolone if their sputum contained eosinophiles in significant numbers, but of his series of 90 cases only 63 showed more than a negligible number of eosinophiles in the sputum. May and Oswald (1957) reported excess of eosinophiles in the sputum of a proportion of cases of chronic bronchitis.

There is thus no alternative to a clinical diagnosis.

Criteria of Successful Treatment

In reports of continuous antibiotic treatment in chronic bronchitis the thesis has been advanced that such treatment, though expensive, could justify itself by reducing the drain on national resources in other ways, *e.g.* from National Insurance payments, and loss of earnings and higher productivity.

For the most part, the trials on which these reports were based did not include any evidence as to the actual economic effect of the treatment given.

Elmes *et al.* (1957) studied the economic effect of treating chronic bronchitis by prompt treatment with an antibiotic of each and every exacerbation, rather than by continuous therapy, and were unable to show any significant economic benefit. They showed the difference between the average patient's estimate of his loss of work due to his bronchitis when directly questioned, and the records of this certified sickness. This finding was confirmed in the present series.

Murdoch *et al.* (1959) and Francis and Spicer (1960) have recently reported therapeutic trials in chronic bronchitis in which an economic criterion was used.

Phear *et al.* (1960) treated 50 patients with "severe chronic asthma" for periods of 3 months to 5½ years with steroids, and claimed significant improvement, in contrast to the conclusion of the Medical Research Council Committee which noted that initial improvement was not maintained.

The group of asthmatics with chronic bronchitis forms a small but important minority of the total bronchitic population; who are apt to become disabled at an earlier stage than the average bronchitic, and who might also have been expected to show a greater response to treatment.

It was for this reason that it was decided to conduct a therapeutic trial limited to this section of the bronchitic population.

This meant an attempt to compare the work lost due to respiratory ill-health over the corresponding period of the previous two years with that lost during the trial period.

Conduct of the Trial

In order to simplify this approach only men under the age of 60 were included, and eventually 60 patients were available for analysis.

Two patients died early in the trial period, and others failed to co-operate adequately or refused to continue.

The trial was made possible by the kindness of Messrs. Upjohn Ltd., who offered supplies of Medrone (Methyl-Prednisolone) and Albamycin T tablets. Each tablet of Albamycin T consists of 125 mg. Novobiocin and 125 mg. Terramycin, and has been shown experimentally and clinically to act as a bacteriostatic antibiotic (1956, 1956, 1957). It is claimed that Medrone (Methyl-Prednisolone) is now known to be an effective steroid in asthma (1957, 1958, 1958).

Many patients were already under intermittent observation, but a full personal and family history was taken afresh, and they were then assessed clinically. Those who were in reasonably good health, both subjectively

and on examination, were admitted as soon as their eligibility had been determined.

Those who were in poor health were admitted to hospital for preliminary treatment directed to rendering them fit for work. Sixteen were admitted to the trial on discharge in this way.

The first patients were admitted in September 1958 and the last in January 1959, in order to make the most valid comparison with former winters. The duration of the trial in the individual case was four calendar months. Each patient was given 3 or 5 weeks supply of tablets, and at each attendance a further supply of tablets was given, and a brief summary of the account of his health and employment during the preceding few weeks was entered on the record. The indirect M.B.C. was also estimated, and the weight and blood pressure were noted. Each patient was provided with a diary, similar to that used by Lawther (1957), to be marked daily, with a letter indicating his condition on that day.

Every man signed an " assent " slip agreeing to the provision of information by the Ministry of National Insurance regarding his Certification of Incapacity during the four months of the trial and the preceding two years, and the Ministry agreed to provide this information on receipt of the " assent " form. On the occasion of the last visit the patient's general impression of the trial period, as compared with the former two or more winters, was recorded.

All patients were provided with Albamycin T and took 500 mg. twice a day, *i.e.* two tablets night and morning. Every man had a number, however, and in accord with this number and a list based on random numbers was issued also with Medrone (4 mg.) or with dummy tablets. These tablets were identical in appearance, and each patient took one tablet three times a day.

It must be made quite clear that the " double blind " was not drawn aside until one month after the last form had been completed. Thus the physician concerned (A.G.O.) did not know what treatment any patient was receiving during the trial.

Clinical Features of the 60 Cases

Table I.—Chronic Bronchitis and Asthma

Maintenance Trial. 60 Cases

CLINICAL DETAILS

Typical asthmatic attacks	49
Allergic manifestations (eczema, rhinitis)	30
Allergic family history	37
Continuous asthma only (though showing exacerbations)	11*

* Six of these gave an " allergic " family history, and three showed other " allergic " manifestations.

Table I shows the clinical features of the series, and it will be seen that the background of allergy is a strong one.

The allergic manifestations recognised, whether personal or familial, included hay fever, perennial rhinitis, and eczema.

The diagnosis of chronic bronchitis was based on persistent cough and phlegm of at least two years duration.

Of the 60 cases, 29 were worse in winter and 10 in summer. In 21 cases there was no seasonal variation in their symptoms. Thirty-two patients had had one or more severe respiratory illnesses, but in only 9 had such an illness exerted a recognisable effect upon the condition.

The cough was seasonal in 15 (*i.e.* intermittent or absent in three or four months of the year) and perennial in 45. The phlegm was constantly thick and greenish in 8, and thick and yellow in 3. In the remainder it was mucoid, although it was stated to become green or yellow during chest colds.

The following table analyses the physical signs at the beginning of the trial when all were fit for regular, though not necessarily active, work.

TABLE II.—60 CASES

PHYSICAL SIGNS ON ENTRY

Grossly deficient air entry	9
Bronchial stridor	59
Obvious expiratory obstruction	42
Local signs	1
No signs	1

The results of X-ray examination were not remarkable. Apical fibrosis in 4 cases believed to be of tuberculous origin was noted.

In 12 depression of the diaphragm and abnormal transradiancy of the lungs led to a radiological diagnosis of emphysema, but in the remainder no significant abnormality was noted.

SIDE EFFECTS

Side effects were mostly mild but in two were troublesome, severe skin eruptions causing the patients to abandon the trial.

The mild side effects were slight looseness of the bowels and minor flatulence and " acidity " with heartburn. The patients were usually delighted with the bowel action, noting that their bowels were moving with greater ease than for many years.

The mild digestive symptoms were usually well tolerated, Aludrox being very effective.

A few patients tolerated the Albamycin T badly, complaining of nausea or diarrhœa, and in these Terramycin was substituted successfully. Two patients complained of depression, but in one this passed off quickly, and in the other it was reported only at the end of the trial.

Two patients complained of severe limb pains, but these again were reported only at the end of the trial: and the same applies to a further patient who became slightly œdematous. The more severe difficulties that affected 18 patients are set out in Table III.

It should be made clear that a number of other patients felt that they were on the whole less well than they had been when they entered the trial, and that some had chest colds during the four months, but these are not included in the table.

In the 18 patients referred to, however, the deterioration was pronounced and the men blamed the tablets. The policy adopted was to agree to change

TABLE III.—CASES DETERIORATING DURING TRIAL

No. of case	*Group*	*Action taken*	*Stage of trial*
70	Dummy	Prednisone Subst.	End of 1st month
29	"	" "	" "
2	"	" "	" "
61	"	" "	" "
65	"	" "	" "
77	"	" "	" "
31	"	" "	" "
55	"	" "	" "
75	"	" "	End of 2nd month
39	"	" "	" "
13	"	" "	" "
73	"	" "	End of 3rd month
*52	"	" "	End of 1st month
72	Medrone	" "	End of 3rd month
23	"	" "	" "
78	Dummy	None	" "
30	Medrone	"	" "
36	"	"	" "

* This man was advised Prednisone, but did not take it: this is referred to in the text.

the treatment if demanded by the patient (provided that there was clinical justification for his complaint). This occurred in 15, of whom 12 complained that they feared the loss of their job, and 3 said that they were not prepared to continue. It was felt that it was unethical to insist on the completion of the trial course under these circumstances, and possibly the patient would cease to attend. It was necessary to keep these patients under observation, even although their future treatment was known, as this group yielded information essential for analysing the effects of treatment. They were all given Prednisone in substitution and the antibiotic was continued. In 8 cases the treatment had to be so changed at the end of the first month, and in three after the second month. When the blind was drawn aside all were found to be receiving dummy tablets. In 3 cases treatment was changed after the third month. Two of these were "Medrone" cases, and one a "dummy" case. One man, who refused to continue the trial, was given Prednisone at the end of the first month, but did not attend again until the end of the fourth month, despite requests to do so. It was then discovered that he had not taken the steroid, but had taken Choledyl prescribed by his doctor. Finally it was found that he had been originally allocated to the "dummy" treatment, and he has therefore been included.

Three further cases who deteriorated expressed willingness to continue the trial. All reported the change in symptoms only at the end of the third month. Two were "Medrone" cases and one was receiving "dummy" treatment.

The main criterion of the success or failure of a treatment was the number of days lost from work, based on the man's claims for sickness benefit, and a diary similar to that introduced by Lawther (1957) marked each day with a letter as follows:

A I am better than usual and at work.
B I am the same as usual and at work.
C I am not so well as usual, but am at work.
D I am not well and am not at work.

By the use of a random list 71 patients were allocated to the two treatments: 33 to Medrone and antibiotic and 38 to dummy tablets and antibiotic. Nine (3 on Medrone and 6 on dummy) were unco-operative and can be referred to as non-starters. One patient in each group died during the course of treatment. Thus there were 29 patients on Medrone and 31 patients on the dummy tablets with records for analysis.

That the two groups were initially comparable is shown in Table IV.

TABLE IV.—COMPARISON OF THE TWO GROUPS BEFORE TREATMENT

	Medrone group	*Dummy group*
Number of men (survivors)	29	31
Age: Under 40	7	7
40-49	9	11
50-60	13	13
Average age	46 years	47 years
Average weekly earnings*	£11 4s.	£11 7s.
Average absence in four winter months** ..	22·5 days	22·7 days

* Excludes men who gave no information on their earnings, but who would suffer no financial loss when ill.

** Averaged over the same four-monthly periods in each of the two previous years.

The age distributions were almost identical, earnings were similar and the records of their absences showed that the average absence (per four months) was 22·5 days for the Medrone group and 22·7 days for the dummy group. These figures are based on the M.P.N.I. records for the four months in each of the two previous years which corresponded to the four months of treatment in the present trial.

The most noticeable difference between the groups under treatment was the frequency of relapse sufficiently severe to necessitate change of treatment. Twelve of the 14 men who changed treatment were having the dummy tablets and only two were having Medrone. Details of these patients and the action taken in each are given in Table III.

Discrepancies between the absences from work recorded in the patients' diaries and those supplied by the Ministry were sufficiently large to demand separate analyses for the two sources of data.

Assessment of the men whose treatment was changed (mostly from the *dummy* treatment, when their condition was deteriorating) is important. This is a different situation from that encountered in other trials when a change from the *active* treatment is necessary because of drug sensitivity. In such trials it has become customary to report the incidence of drug sensitivity, and then to base the comparison between drug and placebo (or between different drugs) on the patients who were able to complete the course of treatment. The justification for such analysis is that drug sensitivity is assumed to be unrelated to the severity of the disease, and that patients who complete treatment are a random

sample in terms of severity. They can then legitimately be compared with patients on other drugs or the placebo.

In the present trial the phenomenon of " placebo resistance " is definitely related to the severity of the disease: for those who did not change from the dummy treatment averaged 12·4 days of sickness, while those who did averaged 33·4 days. Accordingly, the exclusion of those who changed from the dummy treatment would introduce a bias in favour of the dummy treatment and against Medrone.

On the other hand, the inclusion of the total absence records of the patients who changed treatment is also a possible source of bias against Medrone. As soon as their deterioration became intolerable, they were changed to treatment with prednisone. If this had been effective their sickness absence rate would have decreased, and the analysis would have attributed the lower rate to the dummy treatment. No such decrease in absence was observed and an analysis of results for all patients who started on the dummy treatment, compared with all who started on Medrone, gives an unbiased result.

Table V shows the frequency distribution of days absent, according to the Ministry of Pensions data. There is a very wide spread of results, one man being absent for 113 of the 120 days during which he was receiving treatment and 12 from each group having no absence. Nine of the dummy and seven of the Medrone patients had more than one month off sick. The mean number of days absent were 14·1 days on Medrone, and 21·4 days on dummy. In order to test the significance of the difference the distributions were " normalised " by taking the logarithm of the number of days absent plus one (*cf.* Quenouille, 1950). (This transformation reduces the exaggerated importance of the few extremely long periods of absence.) The *t*-test shows that there is no significant difference: $t = 0{\cdot}961$, $d.f. = 58$, $p = 0{\cdot}3$.

A more useful estimation of the effect of treatment can be gained by taking into account the man's absences in previous years. Changes in weather and the increase in age mean that all the difference between current and previous experience cannot be ascribed to the current treatment. Nevertheless, these factors are present to the same extent for both Medrone and dummy patients, and the difference is a valid measure of the effect of Medrone over the corresponding four monthly periods of the previous two years.

The average improvement for Medrone cases is 8·1 days, with a standard error of 5 days. The average improvement for dummy cases is 0·7 days, with a standard error of 5·1 days. Thus neither dummy nor Medrone shows a significant improvement over previous experience, nor is the difference between them of 8·8 days significantly different from zero (the standard error of the difference being 7·2 days).

That Medrone does not significantly reduce sickness absence is valid on the assumption that the patients who changed treatment from dummy tablets to prednisone can be regarded as being controls just as if they had completed their course of dummy treatment. In other words, the assumption is justified if the Prednisone was no more effective in reducing sickness absence than the dummy treatment.

For each of the fifteen men who changed treatment in this way, two percentages were calculated to show the effectiveness of each form of treatment. These were the days absent when on dummy tablets related to the total time on dummy tablets, and the days absent when on Prednisone related to the total time on Prednisone. Various methods of comparing the percentages confirmed that the difference was not significant, but we do not regard this test in the fifteen men as providing a satisfactory trial of Prednisone in this condition.

Thus far, the analysis of absence has been based upon the absences recorded at the Ministry of Pensions. The data from the diaries differed in several instances, although, unfortunately, diaries were not available from all who changed treatment. This analysis will show the effect of the difference between the two sources of data in the groups which did complete their prescribed courses of treatment.

Those on dummy treatment showed almost the same figures with both sources of data. For those on Medrone, however, only 7·6 days average absence was reported in the diaries, against 12·6 days according to the Ministry records. Only eight of these twenty-seven men reported any absences in the diaries, although Ministry records showed claims from sixteen of them.

TABLE V.—DURATION OF SICKNESS ABSENCE DURING THE TREATMENT PERIOD OF FOUR MONTHS

Number of days sickness absence	*Patients who started on*	
	Medrone	*Dummy*
0	12	12
1- 6	7	2
7- 13	1	3
14- 20	2	2
21- 27	—	3
28- 34	1	2
35- 41	2	1
42- 48	1	1
49- 55	1	1
56- 83	2	3
84-111	—	—
112-120	—	1
Total	29	31

THE EFFECT OF THE ANTIBIOTIC

No significant reduction in sickness absence is shown to be produced by the Medrone, but all patients were also receiving maintenance treatment with antibiotics. A crude analysis of the effect of the antibiotic indicates that the average time lost was 3·6 days less than in the previous corresponding periods. This improvement is not statistically significant, and we have data to show the general rate of change of sickness absence from bronchitis.

This therapeutic trial is probably the first of its kind restricted to the asthmatic with chronic bronchitis. The trial by Elmes, Fletcher and Dutton

(1957) was concerned with the intermittent treatment of exacerbations of chronic bronchitis, but was the first such trial to be subjected to an economic "check." Since then, Murdoch (1959) has reported a study judged by work lost from respiratory disease, and the Tuberculosis Association's Committee (Francis and Spicer, 1960) has published a similar report. These two series were composed of chronic bronchitics without asthma.

In the short-term trial by one of us (A.G.O.), previously mentioned, in asthma with bronchitis, a high proportion of patients (72 per cent.) was strikingly improved by combined treatment for a short period.

Albamycin T consists of Novobiocin and Terramycin in equal proportions. Novobiocin has been shown to be effective against the pneumococcus, staphylococcus and *Hæmophilus influenzæ*, and Terramycin has already been widely used in trials similar to this, and been accepted as a valuable therapeutic agent.

The combined treatment might perhaps, over a period of years, have been shown to exert a greater influence on the disease than appeared during the more limited period of four months.

However, the hope and expectations that the asthmatical bronchitic might show better results from maintenance treatment than the ordinary bronchitic has not been borne out. The doubt as to the validity of ministerial figures suggested by Murdoch's experience does not invalidate the above conclusion.

Even if we accept the verbal evidence of the patients and their diaries the gain from the treatment was not striking.

Nevertheless, an effect of Medrone not shown by the criterion used is suggested by the evidence in regard to those patients whose condition forced a change of treatment during the trial.

Of this group of 18 patients, 15 demanded a change of treatment which was agreed to, but the other 3 only had a month to go and were prepared to continue.

A reconsideration of the whole series in the light of all available information concerning the treatment at the time of entry into the trial in addition to the "trial" treatment itself, in each case, yields evidence suggesting a reasonable explanation.

A number were receiving steroid therapy from their doctors at the time of entry. Sixteen were admitted to hospital for intensive treatment to enable them to enter and were therefore having similar treatment.

TABLE VI

Previous treatment	*Trial treatment*		*Totals*
	Medrone	*Dummy*	
Steroid	20 (2)	15 (9)	35 (11)
No steroid ..	11 (2)	14 (5)	25 (7)
Totals	31 (4)	29 (14)	60 (18)

Note: The figures in brackets indicate those who deteriorated severely during the trial.

An analysis of the whole series from this angle is presented in Table VI.

From this it will be seen that 35 patients were receiving steroid (10 mg. Prednisone daily in all cases). Fifteen of these were allocated to dummy treatment and 20 to Medrone. Of the " dummies," 9 showed deterioration (4 during the first month) and 6 showed no very obvious change. Of the 20 allocated to Medrone, only 2 showed obvious deterioration, and that not until the third month.

Of those having no steroid 14 were allocated to dummy treatment, and 5 showed deterioration (all in the first month).

Eleven were allocated to Medrone, and again 2 only suffered an adverse change, both during the third month.

These observations suggest that although Medrone has no pronounced effect in preventing sick absence, it does exert some other clinical effect. The change on entry from the maintenance dose to dummy tablets seems to be associated with a significant deterioration (the difference between 9/15 and 2/20). On the other hand, the comparison of those in whom the change in treatment on entry was in the opposite direction is not significant (2/11 and 5/14).

These comparisons indicate that maintenance treatment by steroid has some clinical effect on certain of these patients, which may be annulled by discontinuing it, a view supported by the frequent clinical observation that deterioration in the chronic asthmatic with chronic bronchitis occurs much more readily than the reverse change.

Phear *et al.* (1959) recently treated 50 patients with " severe chronic asthma " with various steroids over a number of years. They claimed " good " results in 39 of these on a clinical assessment. In only 11 was a " double blind " method used, dummy tablets being substituted without the knowledge of the patient or the physician. This led to significant deterioration in the " dummy " cases. The result seems to be analogous to the changes in treatment initiated at the beginning of the trial period in our cases.

The Medical Research Council Sub-Committee was unable to demonstrate the maintenance of an initial improvement in a series of chronic asthmatics treated by cortisone, although a different method was used.

Hitherto, most reports on therapeutic trials carried out on an out-patient basis have relied on patients' own reporting of results, checked only by close questioning. It is generally considered that any misreporting is likely to affect both groups equally in a trial of the " double-blind " type, so that the assessment of the result is not affected, but apparently this is not always so.

Elmes *et al.* (1958) carried out a therapeutic trial in chronic bronchitis which appeared to yield a favourable result. When information as to the sick absence of the patients from the Ministry of National Insurance became available, however, no significant improvement could be shown. The misreporting in this instance was in the direction of an underestimation of sickness, which happened to favour the antibiotic rather than the dummy treatment.

The present series illustrated this difficulty. Three parallel methods of assessing the results of treatment were used.

The estimates given by patients themselves were made in response to

questioning on the occasion of each monthly visit, the final one being a general impression of the result of the treatment as compared with the previous winter. They agreed with the diaries.

In 37 cases the diaries corresponded closely with the picture presented by the actual records of certification. But in 20 there was definite and sometimes gross discrepancy, which in 19 was in the direction of an under-estimation of the amount of sickness as certified. In 3 other cases there was slight or moderate discrepancy. Thus the diaries and the Ministry agreed closely in 62 per cent., disagreed in 33 per cent. and were in fair agreement in 5 per cent. This amount of inaccuracy can cause faulty estimation of a therapeutic effect. Twelve of the conflicting reports were given by patients receiving dummy treatment, and 8 by those receiving Medrone.

There was a similar discrepancy, although this time in the opposite direction, between the patients' recollection of their absence from work over the two preceding winters, and the ministerial records of incapacity.

This failure in individual assessment indicates the need for a very careful check on all sources of information in therapeutic trials conducted on an out-patient basis. A close personal liaison with the local office providing the records of incapacity is necessary.

Summary and Conclusions

Sixty men under the age of 65, suffering from persistent asthma and chronic bronchitis, were treated by a combined regimen of a known antibiotic, Albamycin T, and an unknown tablet, which was either Methyl-Prednisolone (4 mg.) or a dummy, over a trial period of four winter months.

The criteria of selection for the trial were simply fitness for the job on entry, and a report by the patient of a reasonable amount of loss of work over the preceding two winters, during the months corresponding to those of the trial period.

A clinical analysis of the cases showed a strong personal and/or hereditary allergic background.

The sole criterion of improvement recognised was a comparison of the amount of sick absence during the trial period as compared with the two preceding winters.

Eighteen patients showed severe clinical deterioration during the trial. It was considered necessary to change the unknown tablets in 15 of these to a known steroid tablet (Prednisone) if ethical considerations were to be satisfied. There was strongly suggestive evidence that their respiratory deterioration was related to the treatment they were receiving at the time of entry into the trial.

Discrepancies between the records kept by the patients and those supplied by the Ministry of Pensions and National Insurance regarding absence from work were fairly numerous and applied to 20 per cent. of the cases.

The result of the trial was affected by this discrepancy, but even had the most favourable estimate been accepted the economic gain would have been relatively slight.

At present costs, the use of Medrone would show no economic gain according to the Ministry's results. It is considered to be inadvisable to rely on diaries kept by the patients, in assessing work loss in future therapeutic trials.

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LUNG BIOPSY IN SARCOIDOSIS

WITH SPECIAL REFERENCE TO BACTERIOLOGICAL AND MICROSCOPIC FEATURES

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During the past few years a group of patients, most of whose chest radiographs showed the abnormality of disseminated miliary or patchy shadowing, have been investigated at Brompton Hospital by lung biopsy carried out through a limited thoracotomy incision. The findings in 16 such patients who proved to be suffering from sarcoidosis are reported in this paper, with particular reference to the morbid anatomy, bacteriology, and correlation between the pathological and radiological changes. Eleven patients were under the care of Dr. J. L. Livingstone, and in one of these lung biopsy was performed at King's College Hospital; the remaining five were under the care either of Dr. W. D. W. Brooks or Dr. F. P. Lee Lander.

Material and Methods

The findings for 9 females (aged 21 to 63 years) and 7 males (aged 24 to 42 years) are summarised in Table I and described later in some detail. The lung biopsies were carried out between January 1952 and November 1958 and, with the exception of one of the earliest cases, in whom a formal thoracotomy was performed, the technique employed was essentially similar to that of Klassen, Anlyan and Curtis (1949). Under endotracheal anæsthesia a 4-inch incision was made, usually in the fourth interspace, and the pleural cavity entered either by cutting the intercostal muscles or by stripping a rib and incising the periosteum of the rib bed. The biopsy was taken from the lower border of a lobe, usually middle or upper, held in a Duval clamp. A catheter was inserted into the pleural cavity to aspirate air while the wound was sutured, and then withdrawn, no drainage tube being left in the majority of cases.

It had originally been intended by Dr. J. L. Livingstone that all biopsy specimens from patients under his care would be divided, part being placed in formol-saline for section, and the remainder being sent to the laboratory, preferably immediately and dry, or alternatively in Ringer's solution or normal saline, for culture and guinea-pig inoculation. Unfortunately, for a variety of reasons, *e.g.* the whole specimen being inadvertently placed in formol-saline, bacteriological examination was in fact carried out in only seven specimens. Sections 5 μ thick were stained with hæmatoxylin and eosin by the Ziehl-Neelsen method, Verhoeff's elastic counterstained with Van Gieson, and Gomori's reticulin stain. In 1959 all the sections were reviewed by one of us (L.R.) and examined by fluorescent microscopy for *Mycobacterium tuberculosis* (with negative results in every case).

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Clinical Features

The main clinical features are shown in Table I. They varied from none at all (as where diagnosis followed mass radiography) to a picture clinically indistinguishable from an acute tuberculous pneumonia (Fig. 1). Two patients developed spontaneous pneumothoraces, one a pleural effusion (Fig. 2), two gave a history of erythema nodosum, and in one other there was evidence of generalised sarcoidosis with splenomegaly and hepatomegaly. Common symptoms were cough, wheezing, breathlessness and loss of weight. The Mantoux reaction was positive to 10 T.U. in one, to 100 T.U. in three, and negative to 100 T.U. in the remaining patients.

Radiographic Changes

The radiographic abnormalities varied greatly in type and intensity. In two patients the only abnormality was bilateral hilar node enlargement; abnormal shadows were present in the peripheral lung fields in all the remaining fourteen, in five of whom it was associated with bilateral hilar node enlargement, but appearances ranged from a minimal number of discrete 1-2 mm. opacities in the upper zones in one case, to a dense uniform miliary infiltration in another. The commonest type of infiltration consisted of variable numbers of 1-5 mm. opacities tending to form agglomerations of up to 2½ cm. with rather woolly edges. Associated with this a fine or coarse reticular pattern was sometimes found, and in two patients this combination resulted in a radiological report of honeycomb shadowing. Larger areas of opacity were seen in three cases; in one they were bilateral and confluent in the mid-zones, in another consolidation of the middle lobe occurred, probably due to secondary staphylococcal infection peripheral to stenosed bronchi, and in the third confluence of opacities sufficient to suggest patches of bronchopneumonia. The pleural effusion and two spontaneous pneumothoraces already mentioned gave rise to characteristic radiographic appearances. In one patient bronchography showed definite evidence of multiple bronchostenosis.

The interval between the first symptoms or known radiographic changes, and lung biopsy, varied for fourteen patients from two months to approximately three years. The remaining two gave a history of many years chronic bronchitis and in them it was not possible to estimate the probable duration of sarcoidosis. The total duration of radiographic abnormalities from the beginning of observation is also difficult to estimate accurately, as it is not easy to decide for certain when the radiographic appearances are again normal. However, in two cases the radiograph seemed normal after six months, in two after one year, two after two and a half years, and in one after four years. (The abnormalities in this last patient cleared, relapsed after pregnancy, and cleared again.) The radiographic appearances were still abnormal among the remainder after 1, 2, 2, 2½, 4, 4, 6, 7 and 7 years respectively.

Pathological Features

In the two patients with bilateral hilar node enlargement and clear lung fields, no naked eye changes were found at thoracotomy. In all the remainder

the lungs were studded with variable numbers of grey or yellowish nodules, firm to the touch and varying from a pin-head to a pea in size. In case 5, who had recently had bilateral spontaneous pneumothoraces, bullæ—mostly small—were found on the surface of the lung.

Microscopically large numbers of typical sarcoid lesions were observed in all except case 10 (one of the two patients with bilateral hilar node enlargement and clear lung fields), and in this specimen lesions were present in a hilar node.

The appearance in different sections varied widely; in case 16 and to a smaller extent in case 9 there was sufficient involvement of alveoli to give a picture of consolidation, in case 7 the degree of alveolar involvement was moderate, and in cases 1 and 14 only scattered small foci were found. In several, lesions appeared to be located chiefly in the peribronchial, perivascular and pleural lymphatics. Sarcoid tissue often ensheathed a vessel completely, lying close against the media, while in some cases the latter was replaced with complete loss of elastic fibres. Hyalinisation of the lesions was occasionally a prominent feature, and did not always appear to be closely correlated with the duration of symptoms. A feature of interest was the occurrence in the hilar nodes of cases 10 and 14 (the two patients with radiographically clear peripheral lung fields) of areas of necrosis which, with hæmatoxylin and eosin stain, resembled caseation. These are discussed further in a later section. No tubercle bacilli were demonstrated by fluorescent microscopy in these sections. Cases exhibiting features of special interest are discussed in the following paragraphs.

Recovery of *Mycobacterium Tuberculosis*

Culture of biopsy material for acid-fast bacilli was carried out in 7 cases and guinea-pig inoculation in 3 of these. In one patient both tests gave positive results, and *M. tuberculosis* was also recovered from gastric washings. Sputum or gastric lavage material was cultured on several occasions in all patients, and in one a positive culture was obtained from one of six sputum specimens taken four years after lung biopsy.

Case 1. A 21-year-old girl developed a right-sided pleural effusion in October 1951 (Fig. 2). The only additional radiographic abnormality at that time was a calcified scar at the left apex. Pleural fluid was negative on culture for *M. tuberculosis* and her Mantoux reaction was negative to 1 T.U. (the only strength used). After six weeks' bed rest she was discharged, the effusion having been absorbed, and she resumed work as a typist in January 1952, during which year she remained well, although patchy infiltration developed throughout both lung fields (Fig. 3). On admission to Brompton Hospital in January 1953 there were no abnormal physical signs, and her Mantoux test was negative to 100 T.U., but gastric lavage gave a positive culture of *M. tuberculosis*. Lung biopsy was carried out on 21.3.53, when the lung was found to be studded with numerous firm nodules 2-15 mm. in diameter. Tissue was taken from the middle lobe. Histologically the section, which was about 1·5 cm. in diameter, showed eight sarcoid lesions, the largest being 2 mm. in diameter (Fig. 4). They were scattered irregularly, mainly in peribronchial and perivascular

TABLE 1.—RESULTS OF LUNG BIOPSY IN 16 CASES OF SARCOIDOSIS

Case No.	*Sex*	*Age*	*Main clinical features*	*Mantoux*	*Presence of M. tuberculosis*	*Radiographic appearances*	
						Lung fields	*Hilar nodes*
1	F	21	Pleural effusion	−ve 100 T.U.	G.L. +ve Biopsy culture +ve Biopsy guinea-pig +ve	Calcified apical scar. Right pleural effusion followed by scattered woolly opacities	−
2	F	21	Erythema nodosum, slight breathlessness	−ve 100 T.U.	—	Minimal 1 mm. opacities upper zones	+
3	F	23	Cough, sputum, dyspnœa, wheezing	−ve 100 T.U.	Sputum culture +ve	Fine bilateral mottling mid and lower zones	−
4	F	26	Nil	−ve 100 T.U.	Biopsy culture and guinea-pig −ve	Fine reticulation and mottling, clearing, and recurring after pregnancy	—
5	F	28	Recurrent bronchitis, bilateral spontaneous pneumothoraces	−ve 100 T.U.	Biopsy culture −ve	Confluent linear and confluent shadowing	−
6	F	32	Cough, wheeze, right middle lobe pneumonia beyond bronchostenosis	−ve 100 T.U.	—	Bilateral mottling with some confluence in right middle lobe	−
7	F	48	Cough, breathlessness	+ve 100 T.U.	—	Bilateral upper and mid zone mottling	+

8	F	55	Loss of weight, splenomegaly, heptamegaly, Sjögren's syndrome	−ve 100 T.U.	Biopsy culture and guinea-pig −ve	Generalised mottling and reticulation	−
9	F	63	3 years cough wheeze then clinical pneumonia followed by progressive dyspnœa, harsh cough and wheezing	−ve 100 T.U.	—	Bilateral honeycomb shadowing and patchy clouding	—
10	M	24	Erythema nodosum, lassitude	−ve 100 T.U.	—	Clear	++
11	M	25	Cough, loss of weight	−ve 100 T.U.	—	Generalised peripheral fine mottling and reticulation	−
12	M	28	Slight persistent cough	−ve 100 T.U.	Biopsy culture −ve	Generalised woolly mottling	+
13	M	34	Cough, sputum, wheezing, dyspnœa. Right spontaneous pneumothorax 2 years after lung biopsy	+ve 100 T.U.	—	Bilateral fine upper zone mottling and streaking	−
14	M	35	Recurrent slight hæmoptyses, cough, loss of weight	−ve 100 T.U.	Biopsy culture −ve	Clear	+
15	M	37	Bilateral chest pains, dyspnœa	+ve 100 T.U.	Biopsy culture −ve	Dense bilateral miliary infiltration	+
16	M	42	Clinical picture of acute pneumonic pulmonary tuberculosis	+ve 10 T.U.	—	Dense bilateral upper and mid zone infiltration and consolidation	+

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4	F	26	Nil	−ve 100 T.U.	Biopsy culture and guinea-pig −ve	Fine reticulation and mottling, clearing, and recurring after pregnancy	—
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lymphatics with one small granuloma in a pleural lymphatic. The central part of several of the lesions showed dense eosinophilic material which was shown by special stain to be collagen. A portion of the biopsy specimen was cultured and gave a growth of 20 to 100 colonies of *M. tuberculosis*. A further portion was ground in a Griffiths tube with sterile sand and penicillin water and 2 ml. of the filtrate was injected into the hind leg of a guinea pig. The animal did not develop generalised tuberculosis, but *M. tuberculosis* was cultured from pus aspirated from an inguinal gland. A six weeks course of streptomycin was given without any notable effect on the radiographic abnormalities, but these gradually disappeared over the next 9 months and have not recurred (Fig. 5).

Case 3. This was a much more common type of case. A 23-year-old woman who developed cough, breathlessness on exertion, and wheezing, was found on radiography to have fine mottling in both mid and lower zones. Sputum was repeatedly negative on culture for acid-fast bacilli and her Mantoux reaction was negative to 100 T.U. Lung biopsy showed numerous granulomata characteristic of sarcoid, particularly within alveolar walls, and, in some parts, confluent so that the lung was consolidated. No special treatment was given. Four years later there was a slight increase in the extent of radiographic infiltration and one of six sputa gave a positive culture for *M. tuberculosis*, the Mantoux reaction remaining negative to 100 T.U. She was put on anti-tuberculous chemotherapy, but little radiographic change occurred during the next two years. Her erythrocyte sedimentation rate has always remained in the region of 50 mm. in one hour (Westergren).

Discrepancy between Radiographic Appearances and Pathological Findings

In most patients there was a reasonable degree of correlation between the intensity of the radiographic and pathological changes, but in two there was a marked discrepancy.

Case 14. A 35-year-old porter who had produced a trace of frothy blood-stained sputum about once a year for five years complained of the loss of 2 stone in weight, lassitude, cough, and slight breathlessness on exertion during three months prior to admission to Brompton Hospital. His pupils were unequal, irregular and reacted poorly to light, and the Wassermann and Kahn reactions were positive. A chest radiograph showed bilateral hilar node enlargement with clear lung fields (Fig. 6). Seven specimens of sputum were negative on culture for *M. tuberculosis* and the Mantoux reaction was negative to 100 T.U. At biopsy in August 1957 the lung appeared normal macroscopically, but microscopically occasional small granulomata were present both in alveolar walls and perivascular and peribronchial sheaths. A section of an enlarged hilar node (Figs. 7, 8 and 9), also removed, was 2 cm. in length and almost entirely replaced by tubercles, mostly non-caseating, but with several areas of granular necrosis identical in appearance with caseation. This finding is discussed later. Culture and guinea pig inoculation of the biopsy specimen gave negative results. Anti-tuberculous chemotherapy was given, but eight months later, in spite of continuing this treatment, scattered opacities appeared in the peripheral lung fields, while the hilar node enlargement largely regressed (Fig. 10).

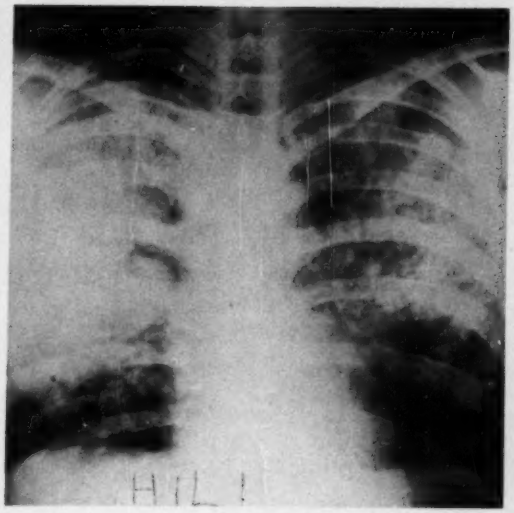

FIG. 1.—Case 16. Radiograph showing upper and mid-zone consolidation. The abnormal shadows had almost completely cleared eight months later.

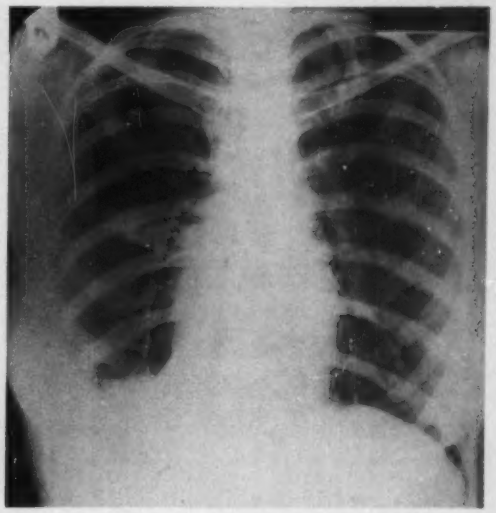

FIG. 2.—Case 1. Absorbing right pleural effusion. Calcified scar at left apex. Lung fields clear.

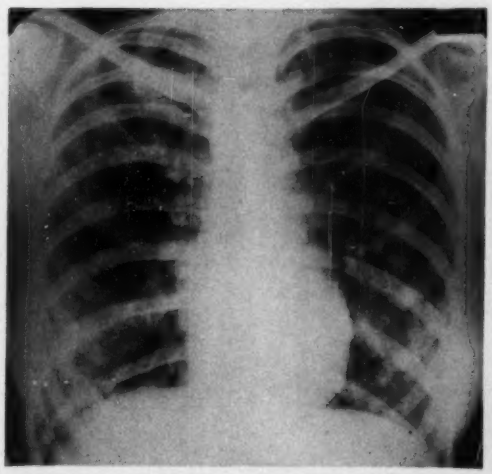

FIG. 3.—Case 1. Radiographic appearances one year later, showing bilateral disseminated patchy infiltration. Lung biopsy taken from right middle lobe three months after this film, when the radiographic appearances were similar.

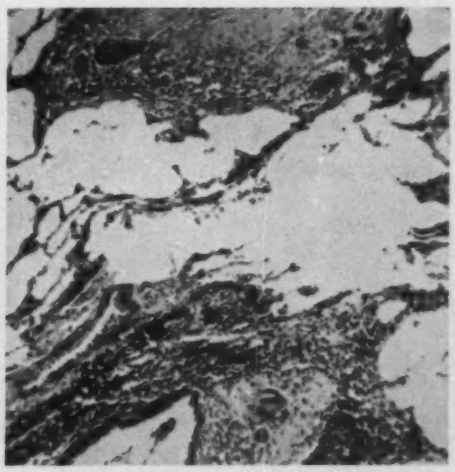

FIG. 4.—Case 1. Photomicrograph showing above sarcoid granuloma with fibrous tissue centrally and cellular granulation tissue peripherally, and below lesion in wall of bronchiole. (Hæmatoxylin-eosin, ×42)

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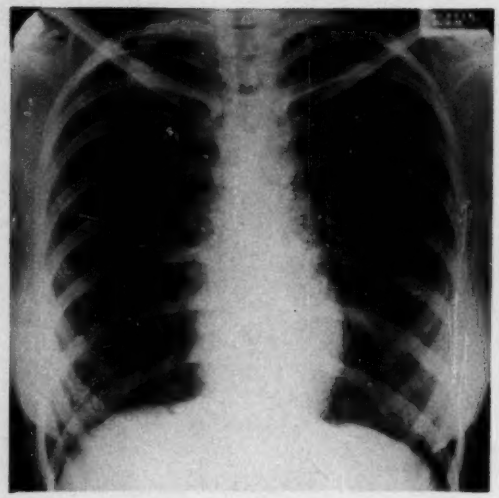

FIG. 5.—Case 1. Appearances nine months after lung biopsy, showing normal lung fields except for the left apical scar.

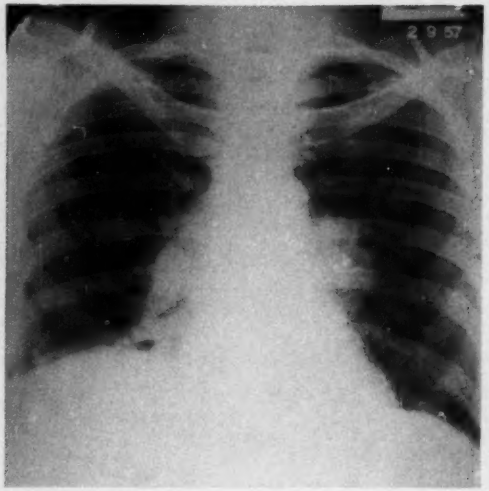

FIG. 6.—Case 14. Radiographic appearances about time of lung biopsy, showing bilateral hilar node enlargement and clear lung fields.

FIG. 7.—Case 14. Photomicrograph showing area of granular eosinophilic material, a small example of several such areas throughout the lymph node—resembling fibro-caseous tuberculosis. (×42.)

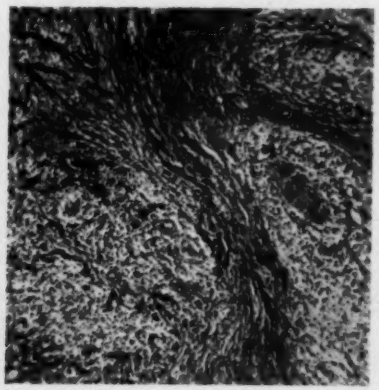

FIG. 8.—Case 14. A section of the same area as that shown in Fig. 7, stained with Van Giesen's stain (for collagen). Through the seemingly necrotic areas collagen fibres are present in large numbers. (×42.)

The patient was also given a course of penicillin because of the positive W.R. In this case, therefore, the microscopic changes preceded the radiographic by many months.

Case 2. A 21-year-old girl who had recently had erythema nodosum complained of lassitude and breathlessness on exertion. Radiographically there were a few scattered 1-2 mm. shadows in the periphery of the upper zones, with bilateral hilar node enlargement. At biopsy the lungs were found to be studded with hard yellowish nodules 1-2 mm. in diameter, and microscopically large granulomata were seen, some in alveoli, others within the bronchial wall. In some places the bronchial epithelium was lost; evidence of chronic collapse was seen in some parts of the lung. These findings were more severe than might have been expected from the slight radiographic abnormalities.

Histological Appearances suggestive of Caseation

As noted above, the hilar node excised in case 14 showed in hæmatoxylin and eosin stained section an appearance resembling caseation. This appearance has given rise to the diagnosis of tuberculosis in several patients referred to us from different centres, although clinically the diagnosis was sarcoidosis.

Case 10. A 24-year-old male who had recently had erythema nodosum was found radiographically to have bilateral hilar node enlargement with clear lung fields. His Mantoux reaction was negative to 100 T.U. and sputum was repeatedly negative on culture for acid-fast bacilli. At biopsy the lung was normal both to the naked eye and microscopically. An excised hilar node was small, about 0·8 cm. in diameter, and was replaced by sheets of hyaline connective tissue, with epithelioid cells and giant cells at the periphery and areas of granular necrosis resembling fibro-caseous tuberculosis (Fig. 11).

In both the above cases the appearance at first sight suggested fibro-caseous tuberculosis, but when the sections were specially stained it was possible to show, by the distribution of reticulin throughout the area of necrosis, and its association with mature collagen, that the appearance of granular necrosis could not be considered pathognomonic of caseating tuberculosis.

Radiographic and Pathological Consolidation

In one patient the clinical, radiographic and pathological features were those of an extensive sarcoid consolidation. In another a bacterial pneumonia developed distal to a stenosed middle lobe bronchus.

Case 16. In June 1952 a 42-year-old radio engineer, whose radiograph (M.M.R.) three months previously was normal, developed marked breathlessness on exertion, lassitude, and cough productive of purulent sputum. A radiograph six weeks later showed confluent shadows in both mid zones and patchy infiltration elsewhere (Fig. 1). He was orthopnœic and there were a few râles at the left base. Left pleural pain and a friction rub developed and the sputum was intermittently bloodstained. The white cell count was 15,000 per c. mm. (89 per cent. neutrophils), and his Mantoux reaction was strongly positive to 10 T.U. He was treated for pulmonary tuberculosis at a local

hospital with streptomycin and PAS for a month, but after fourteen purulent sputa were reported negative for acid-fast bacilli the diagnosis was questioned, treatment was stopped and he was transferred to Brompton Hospital under the care of Dr. J. L. Livingstone. Tomography showed bilateral hilar node enlargement. His sputum gave normal results. At biopsy in October 1952 the lung was indurated and studded with fine yellow nodules the size of a pin-head. Section showed many large granulomata which were confluent, so that the lung was largely replaced by sarcoid tissue (Fig. 12). The patient rapidly became symptomless and steady regression of the radiographic abnormalities occurred, until by June 1953 there remained only some streakiness in the upper zones. Although he was given a further course of 40 g. streptomycin with PAS it was felt that this treatment was not responsible for the symptomatic and radiographic improvement, both of which began several weeks after the end of the first course and before starting the second.

There was one additional factor in this patient's history which, after very careful consideration, was decided to be almost certainly irrelevant. A month before the onset of symptoms three fluorescent lighting strips, each about 5 feet long, fell from a shelf in his office and broke on the floor. They were in brown paper and did not become unwrapped. The patient was aware of the hazard of berylliosis and quickly carried them outside, holding his breath. However, beryllium had ceased to be used in the manufacture of fluorescent lighting in this country some three years previously, and even if present in these strips the quantity which he could have inhaled must have been minute.

Case 6. A 32-year-old married woman, who for several months had complained of dry cough and occasional attacks of breathlessness, in October 1957 developed pneumonia of the right middle lobe, associated with an attack of Asian influenza. Radiography showed bilateral upper zone mottling in addition to collapse and consolidation of the middle lobe. A film two years previously had been normal. Staphylococci resistant to most antibiotics were present in the sputum, which was repeatedly negative for acid-fast bacilli. Clinically and radiographically the middle lobe pneumonia improved on a series of antibiotics (penicillin, polymixin, neomycin and novobiocin), but the upper zone mottling increased. Bronchography showed stenosis of the middle lobe bronchus. She was admitted to Brompton Hospital a year later because of recurrent wheezing and dyspnœa, the radiographic appearances having remained unchanged. Bronchoscopy revealed stenosis of the left lower lobe bronchus and right main bronchus of such degree that an adolescent bronchoscope could not be passed down to inspect the middle and lower lobe bronchi. No bronchial biopsy was done. Lung biopsy showed typical sarcoid lesions with much central fibrosis. In spite of treatment with steroids and antituberculous chemotherapy, wheezing has persisted and some radiographic deterioration occurred.

Spontaneous Pneumothorax

Spontaneous pneumothoraces occurred in two patients.

Case 5 has already been reported as case 3 in the series of Wynn-Williams and Shaw (1957), who describe four cases and review the literature on the subject. She developed successively right and left spontaneous pneumothoraces

a few weeks before lung biopsy, at which, in addition to the usual appearances seen in sarcoidosis, bullæ were found on the lung surface.

Case 13. A 35-year-old man with a history of 3½ years' variable cough, wheeze and breathlessness, had bilateral upper zone mottling on his radiograph. His lung biopsy (following a negative liver biopsy) showed the typical naked-eye and histological lesions of sarcoidosis. He was treated with continuous steroids and anti-tuberculous chemotherapy, but his symptoms were never well controlled, and from time to time transient localised increases occurred in the density of the abnormal shadows in various parts of the lung fields. Eighteen months after biopsy a right spontaneous pneumothorax occurred and only eventually re-expanded after pleurodesis with silver nitrate.

Recurrence of Abnormal Shadows after Pregnancy

A 26-year-old housewife was found on a routine mass radiograph in April 1954 to have bilateral fine mottling combined with a reticular pattern. At lung biopsy the classical naked-eye and microscopic appearances of sarcoidosis were found, with severe pleural, peribronchial, perivascular infiltration and some alveolar involvement, and also patchy emphysema. Culture and guinea-pig inoculation of biopsy material gave negative results. A six weeks course of streptomycin and isoniazid was without effect on the infiltration, which subsequently began to improve spontaneously until by October 1955 the lung fields were practically clear. The patient became pregnant and the baby was born in November 1956, the radiographic appearances remaining normal throughout. In March 1957 intense bilateral miliary mottling was found at a routine examination, although she was symptomless. After three months this began to regress without treatment, and by January 1958 the radiographic appearances were again practically normal.

Discussion

In the present series the age and sex incidence, tuberculin sensitivity, and radiographic appearances with the exception of case 16, correspond with the findings in larger series (Longcope and Freiman, 1952; Hoyle, Dawson and Mather, 1954; Scadding, 1956).

The most interesting patient from the point of view of the relationship between sarcoidosis and tuberculosis is case 1, whose lung biopsy specimen yielded *M. tuberculosis* on culture and gave a positive guinea-pig inoculation test, although Mantoux negative. The guinea-pig did not develop generalised tuberculosis, but *M. tuberculosis* were cultured from pus aspirated from an inguinal gland. The colonies were typical of *M. tuberculosis* of human type, but unfortunately at that time the importance of photochromogens was not recognised and the detailed study necessary to identify these organisms was not made. The calcified scar at the left apex seen on radiography is proof that at some earlier period caseation had occurred, but the organisms were recovered from a small block of material, the whole of which showed histologically classical sarcoid lesions with no evidence of caseation.

The finding of *M. tuberculosis* in patients with sarcoidosis is by no means rare. Thus Scadding (1956) recovered *M. tuberculosis* in 14 out of 142 patients.

In 10 the sputum, gastric lavage material, or laryngeal swabs were positive on culture or on direct examination while the patient was still in the sarcoid phase, the tuberculin sensitivity remaining low, and in one of them *M. tuberculosis* was cultured from the lung at autopsy. Case 3 of the present series would seem to correspond with this group. In the remaining three of Scadding's patients the finding of *M. tuberculosis* was accompanied by a change to a partly caseating phase with increased tuberculin sensitivity. Ricker and Clark (1949) reported one positive culture among 26 autopsy cases in which culture from lung tissue was attempted, and one positive guinea-pig inoculation among 26. Dietrich (1931) found *M. tuberculosis* in skin lesions in two cases, and Schaumann and Hallberg (1941) reported *M. tuberculosis* in sections of lymph node, though culture and guinea-pig inoculation were negative. Riley (1950) used acid-fast stains on sputum and gastric lavage material in 40 patients with sardoidosis, obtaining positive results in four, but subsequent smears and cultures from these four were all negative. Kissmeyer (1932), Hollister and Harrell (1941), and Pinner (1938) collected among them 25 cases, mainly from the literature, of tuberculosis developing in guinea-pigs inoculated with material from sarcoid lesions. The first three of these authors suggested that this was usually the result of unsuspected concomitant tuberculosis and was not proof of a tuberculous ætiology of sarcoidosis. Clearly such an argument is difficult to refute, though it seems unlikely in case 1 of the present series, in whom, as previously noted, the entire block showed nothing but classical sarcoid lesions, *i.e.* non-caseating granulomata. A further unusual feature of case 1 was the occurrence of a large pleural effusion. Although microscopic involvement of the pleura was found in practically every case in the present series, the development of a pleural effusion has not often been reported (Bruce and Wassen, 1940; Reisner, 1944; McCort *et al.*, 1947).

Two cases where hæmatoxylin-eosin stained sections showed caseation, but where more special stain failed to meet certain criteria, were of considerable interest (Figs. 7-9 and 11). Sarcoidosis is defined in terms of the microscopic appearance, one of the main features being the absence of caseation (Scadding, 1950). Since the finding of caseation precludes the diagnosis of sarcoidosis, firm diagnosis on any one section is based on the assumption that the material examined is characteristic of all lesions. This means that the usual report "consistent with the diagnosis of sarcoidosis" is more than a circumlocution. The absence of caseation does not rule out tuberculosis, and its presence—which excludes sarcoidosis—is usually associated, in this country at least, with tuberculosis.

Many early accounts of sarcoidosis dealt largely with biopsy material, but Longcope and Freiman reported that the more autopsy material was examined the more it became necessary to accept a certain amount of "granular necrosis" as consistent with sarcoidosis. Longcope and Freiman describe this form as "spotty," rarely involving more than a few scattered lesions and strictly limited to the central portions of the granulomatous foci. They stress the value of a reticulin stain as it demonstrates reticulin passing right through the area of necrosis.

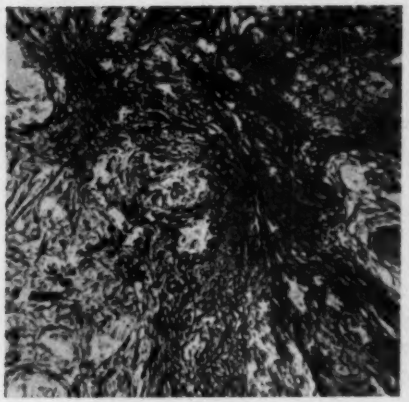

FIG. 9.—Case 14. A consecutive section to that shown in Fig. 8, stained with Gomori's stain (for reticulin). Through the seemingly necrotic areas reticulin fibres are present in large numbers. (×42.)

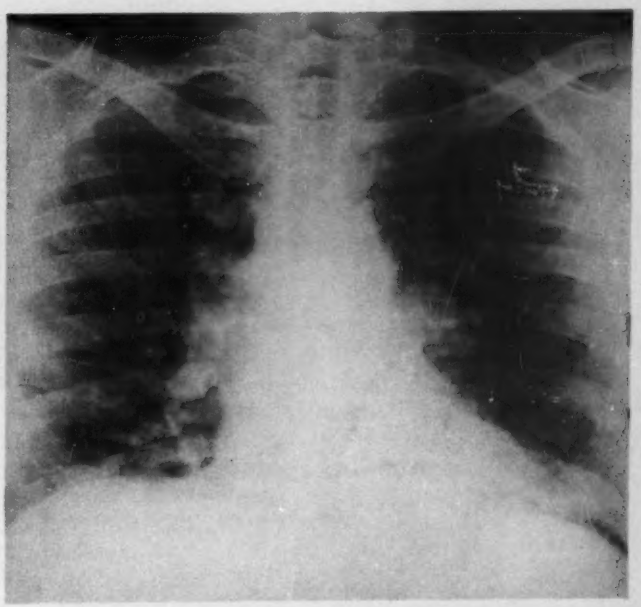

FIG. 10.—Case 14. Appearances eighteen months later, showing bilateral patchy infiltration with regression of hilar node enlargement. The abnormal peripheral shadows first appeared eight months after lung biopsy.

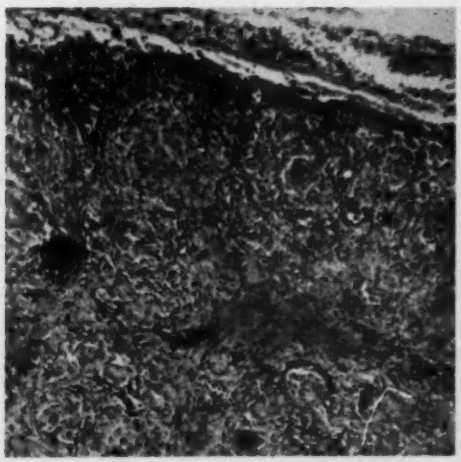

FIG. 11.—Case 10. Stains as in (7). Here the eosinophilic area is larger and granularity again suggests necrosis. Reticulin and collagen more abundant than in (7). (×42.)

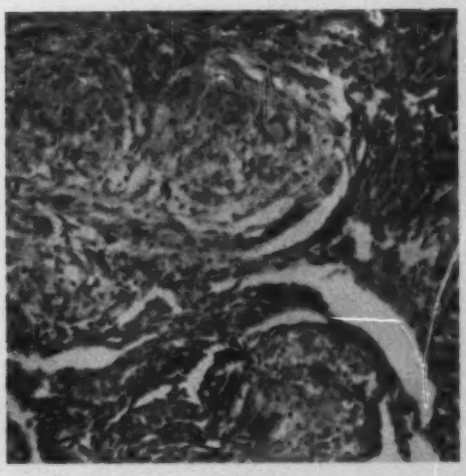

FIG. 12.—Case 16. Photomicrograph showing alveolar walls and spaces almost replaced by sarcoid granulation tissue. (Hæmatoxylin-eosin ×90.)

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In lymph node and lung the granulomata are often large and confluent and, particularly in the early stage of hyalinisation, diffuse sheets of granulation tissue are seen. It is not strange that granular necrosis may be seen at some stage in the evolution of a sarcoid lesion, as initially the lesion is highly cellular, subsequently being replaced by hyaline, which often first appears centrally in a granuloma.

This necrosis has the same appearance in a microscopic section as " caseous necrosis," that " peculiar form of necrosis " which Cameron (1951) describes as cheesy or milky by reference to the naked-eye appearance. In sarcoidosis these necrotic areas are small and unrecognisable to the naked eye; moreover a histological feature distinguishes between " granular necrosis " found in sarcoidosis and the " caseation " of tuberculosis. Nickerson (1937), quoting Medlar (1926), stresses that in sarcoidosis " with silver impregnation a delicate reticulum is always present in the lesion." In tuberculosis this is destroyed by the " onset of caseation." Medlar stresses that reticulin may sometimes be present in caseous areas in tuberculosis, perhaps explaining why cavitation or ulceration does not always occur, but here he is referring to the reticulum or the supporting structure of the organ, rather than to the new formation of reticulin. Longcope and Freiman express similar views on the importance of the presence of reticulin fibres in areas of necrosis in sarcoidosis.

Hyaline material may at first sight resemble caseous material because it is relatively acellular, eosinophilic, and may merge with very active granulation tissue in sarcoidosis (Fig. 8). Special stains (*e.g.* van Giesen) will identify collagen and this, together with a reticulin stain (*e.g.* Gomori's), will help in diagnosis where a hæmatoxylin-eosin stained section fails to do so.

From the practical point of view, the exclusion of caseation was of some consequence in two patients. Case 10 decided not to postpone marriage as he had done when he thought he was suffering from frank tuberculosis, and case 11 was accepted as an immigrant without deferment by one of the Dominions.

The most unusual patient in the series was case 16, because of the severity of the symptoms and density of the radiographic shadows (Fig. 1), which, moreover, cleared more rapidly than is usual in sarcoidosis. Two alternative diagnoses were considered. The clinical and radiographic findings were consistent with tuberculosis, and three acid-fast rods were seen in a Ziehl-Nielsen stained section, though fluorescent microscopy several years later was negative. However, the rapid resolution appeared to be independent of anti-tuberculous chemotherapy, and the pathological findings were typical of sarcoidosis. Berylliosis seemed extremely unlikely as the strip probably did not contain beryllium, and as the maximum dose which could have been inhaled was so small that an extraordinary degree of sensitivity would have to be postulated.

The recurrence of dense radiographic infiltration after complete clearing, such as occurred in case 4, is unusual but has been reported previously (Longcope and Freiman, 1952). It is of interest that the deterioration occurred shortly after parturition. Improvement in the radiographic abnormalities during pregnancy is a well-recognised phenomena in sarcoidosis (Berman, 1951; Aikens and Beckwith, 1955; Maycock *et al.*, 1957; Abitbol, 1958), but in

case 4 of the present series complete radiographic clearing had taken place before the patient became pregnant. Maycock and others (1957) found that after parturition radiographic relapse of parenchymatous lesions occurred in 3 out of 7 women in whom improvement had taken place during pregnancy. Complete regression of the lesions during pregnancy was found in only one of their patients, and in her case relapse occurred after the first, second and third pregnancies, but not after the fourth and fifth. The mechanism involved is not clear.

Since in all patients in the present series the clinical diagnosis was confirmed either from a piece of lung or a hilar node, it would seem advisable at thoracotomy to excise both. A diagnosis of pulmonary or mediastinal sarcoidosis can probably be made always with this policy. Lesions may be found in the lung even in the absence of radiographic evidence of pulmonary infiltration. It is interesting to compare these results with those of Mather, Dawson and Hoyle (1955) for liver biopsy. They obtained evidence of sarcoidosis in 58 of 90 patients whose chest radiographs showed either hilar node enlargement, pulmonary infiltration, or both. However, while positive results were found in 48 out of 64 patients (*i.e.* 75 per cent.) with hilar node enlargement (either alone or combined with lung infiltration), among the 26 patients who had pulmonary infiltration without hilar node enlargement positive results were obtained from only 10 (*i.e.* 39 per cent). Two conclusions seem to follow from these figures; firstly, in patients with pulmonary sarcoidosis, lung biopsy will much more frequently yield a diagnosis than liver biopsy; and secondly, its value will be especially great among those patients with pulmonary infiltration but no hilar node enlargement, in whom liver biopsy is likely to be positive in less than 50 per cent. (as in case 13 of the present series). If liver biopsy is negative in such patients and pathological proof of the diagnosis is desirable, then lung biopsy should be considered.

There were no complications from the operation of lung biopsy in the present series. Among a combined total of approximately 230 operations carried out by essentially the same technique, and for a wide variety of diseases, reported in the series of Klassen and others (1949), O'Donnell (1955), Theodos, Allbritten and Breckenridge (1955), and Effler *et al.* (1955), there appear to have been two deaths, neither of which occurred in patients with sarcoidosis. One was a man suffering from silicosis who was in heart failure prior to the operation, and the other was a 48-year-old man with severe asbestosis who suffered a fatal myocardial infarct on the fifth post-operative day. Terry (1952), analysing the complications of over 10,000 liver biopsies, found a mortality of 0·12 per cent., but again there appear to have been no deaths among patients suffering from sarcoidosis. We think that for patients suffering from sarcoidosis diagnosis by lung biopsy in experienced hands is slight. However, lung biopsy is a more severe operation requiring a skilled surgical team, adequate theatre facilities, and a longer stay in hospital. Moreover, some patients with radiographic pulmonary infiltration submitted to lung biopsy will be found to have some disease other than sarcoidosis, and in them the risks may be greater, especially if much fibrosis is present. Therefore, we do not suggest that lung

biopsy should replace liver biopsy in the diagnosis of sarcoidosis: rather is it a technique to be reserved for selected cases in hospitals with adequate surgical facilities.

Summary

1. The clinical, radiographic and pathological findings are reported in 16 cases of sarcoidosis diagnosed by means of lung biopsy.

2. In one patient there was strong evidence of a tuberculous ætiology.

3. Necrosis resembling caseation was found in hilar nodes excised from two patients. Caseation was however excluded by the use of stains for collagen and reticulum.

4. In one patient the pathological changes preceded radiographic abnormalities by several months.

5. The findings in this series suggest that lung biopsy with simultaneous excision of a hilar node will give a positive diagnosis in practically all patients with sarcoidosis and lung involvement. In particular, lung biopsy is more likely to be successful than liver biopsy in those patients whose chest radiographs show diffuse pulmonary infiltration without evidence of hilar node enlargement.

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SURGERY IN BRONCHO-PULMONARY ASPERGILLOSIS

By J. R. Belcher and N. S. Plummer

From the London Chest Hospital

Little attention has been paid to the surgical problems presented by patients with pulmonary aspergillosis. There are not many relevant reports in the literature and most of these are accounts of single cases of aspergilloma treated by resection.

For some time it has been our impression at the London Chest Hospital that when *Aspergillus fumigatus* has been found in the sputum of patients who have been submitted to surgery, the morbidity rate following operation has been high. This paper is concerned with 21 patients who were operated upon for pulmonary lesions from which the fungus was isolated, and a study of these patients suggests that our impression was well founded, but only in certain types of aspergillosis. The high incidence of post-operative complications in these latter cases is probably due more to the severity of the associated lung disease than to the presence of the fungus.

Definition

The part played by *Aspergillus fumigatus* in broncho-pulmonary disease in man is almost always that of a pure saprophyte, but it is sometimes capable of invading diseased tissues. The fungus has been found in an increasing number of cases presenting surgical problems. These may be divided into three groups: those with aspergillomas; those in which the fungus was found in lung tissue already damaged by chronic infection, but in which no aspergilloma had formed; and those in which the fungus was found in the mucous plugs characteristic of allergic aspergillosis (Hinson *et al.*, 1952). Although this classification is based essentially on morbid anatomical findings, it is usually possible to place individual cases of aspergillosis in their appropriate category on clinical and radiological grounds.

A. *Aspergilloma.* An aspergilloma is a circumscribed mass of aspergillar mycelium contained within the wall of a cyst or cavity in a lung. Radiologically it appears as a solid shadow often surmounted by a crescentic air space or only partly filling a much larger air space. Macroscopically aspergillomas consist of brown putty-like masses lying loose in the cysts or cavities in which they develop. For convenience of description we have divided these cases into two groups: simple aspergillomas and complex aspergillomas, according to the nature and extent of the underlying disease of the lung.

Simple aspergillomas develop in isolated thin-walled cysts of bronchial origin and the formation of these cysts in all probability precedes the formation of the

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ball of fungus (Fig. 1). There is little or no abnormality in the surrounding lung and the cyst wall itself is usually lined by ciliated epithelium. These masses sometimes reach a considerable size.

Complex aspergillomas, on the other hand, develop in cavities with gross disease in the surrounding lung tissue. The underlying lung disease may be chronic tuberculosis, a chronic lung abscess, advanced sarcoidosis, or gross bronchiectasis (Fig. 2). The intracavitary masses themselves are similar to those in the preceding group.

TABLE I.—DETAILS OF OPERATIONS FOR PULMONARY LESIONS WITH FUNGUS ISOLATED

No.	*Age*	*Sex*	*Site of lesion*	*Operation*	*Underlying pathology*	*Complications*	*Aspergillus in sputum before operation*
				SIMPLE ASPERGILLOMAS			
1.	58	M	L.U. lobe	Segment resected	Cyst	None	Positive
2.	25	M	R.L. lobe	Lobectomy	Cyst	B.P. fistula and empyema	Positive
3.	64	M	R.U. lobe	Lobectomy	Cyst	None	Negative
4.	27	M	R.L. lobe	Lobectomy	Cyst	None	Negative
5.	50	M	R.U. lobe	Lobectomy	Cyst	None	Negative
6.	60	M	R.U. lobe	Lobectomy	Cyst	None	Negative
				COMPLEX ASPERGILLOMAS			
7.	17	F	R.U. lobe	Segment resected	Abscess	Air leak	Positive
8.	60	M	R.U. lobe	Lobectomy	Tuberculosis	None	Negative
9.	54	M	R.U. lobe	Lobectomy	Abscess	B.P. fistula and empyema	Positive
10.	37	F	R.U. lobe	Pneumonectomy	Tuberculosis	Empyema	Positive
11.	35	F	R.U. lobe	Lobectomy	Tuberculosis	B.P. fistula and empyema	Positive
12.	49	F	R.U. lobe	Lobectomy	Abscess	Empyema and *death*	Positive
13.	66	M	L.U. lobe	Drainage	Tuberculosis	B.P. fistula	Positive
14.	52	M	L. lung	Pneumonectomy	Tuberculosis	B.P. fistula	Negative
15.	51	M	L.U. lobe	Pneumonectomy	Bronchiectasis	None	Negative
16.	47	M	R.U. lobe	Lobectomy	Abscess and asbestosis	None	Negative
				ASPERGILLAR INFECTION OF SUPPURATIVE LESIONS			
17.	65	M	R.U. lobe	Lobectomy	Suppurative pneumonia	B.P. fistula and *death*	Negative
18.	55	M	R.U. lobe	Lobectomy	Suppurative pneumonia and bronchiectasis	Air leak	Positive
				ALLERGIC ASPERGILLOSIS			
19.	53	M	R.U. lobe	Lobectomy	Bronchiectasis	None	Negative
20.	31	F	R.L. lobe	Segments resected	Bronchiectasis	None	Negative
21.	44	M	R.L. lobe	Lobectomy	Bronchiectasis	None	Negative

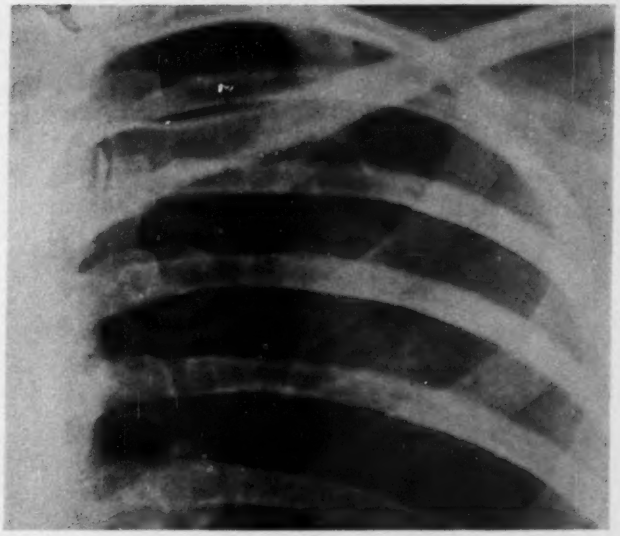

FIG. 1.—Simple aspergilloma. This radiograph shows a solid shadow with the characteristic crescentic air space above it. There is no obvious abnormality in the surrounding lung.

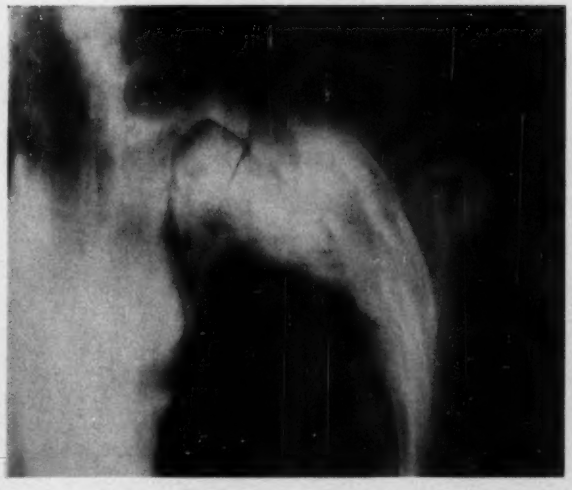

FIG. 2.—Complex aspergilloma. This radiograph shows a solid shadow and a crescentic airspace with obvious gross lung destruction around it.

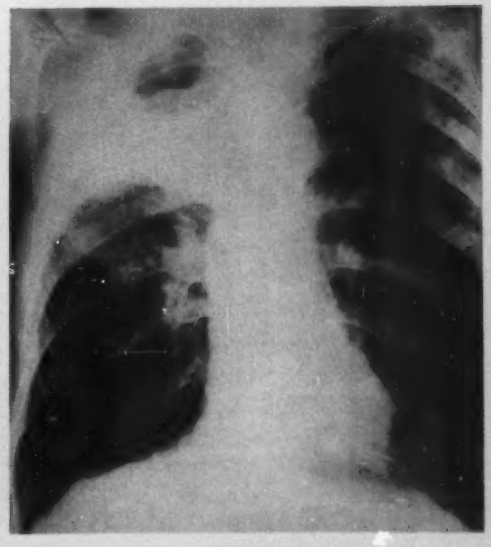

FIG. 3.—Aspergilloma infection. This radiograph shows cavitation and consolidation of the right upper lobe. There is no solid shadow due to a fungus ball, but the mycelium was isolated from the resected specimen.

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Hitherto no distinction has been made between simple and complex aspergillomas, but the results of surgery in the two groups are sufficiently different to make the distinction important from a clinical point of view, quite apart from the basic differences in pathology as indicated above.

B. *Aspergillosis in Pulmonary Suppuration.* In the second group, the fungus is

TABLE II.—CASES FROM THE LITERATURE

Author	*Age*	*Sex*	*Site of lesion*	*Operation*	*Underlying pathology*	*Complications*	*Aspergillus in sputum before operation*
				SIMPLE ASPERGILLOMAS			
Deve	29	M	R.U. lobe	Lobectomy	Cyst	B.P. fistula and *death*	Negative
Gerstl	33	F	L.U. lobe	Lobectomy	Cyst	None	Negative
Yesner	33	M	L.L. lobe	Lobectomy	Cyst	None	Negative
Hochberg	48	M	L.U. lobe	Segment resected	Cyst	None	Negative
Pesle	39	M	R.U. lobe	Marsupialisation	Cyst	*Death*	Negative
	42	M	L.U. lobe	Drainage	Cyst	None	Positive
	35	M	L.L. lobe	Segment resected	Cyst	None	Negative
Hughes	56	M	L.L. lobe	Lobectomy	Cyst	None	Negative
Friedman	55	F	R.U. lobe	Lobectomy	Cyst	None	Negative
Hausmann	52	F	L.U. lobe	Segment resected	Cyst	None	Negative
Vellios	54	M	L.U. lobe	Segment resected	Cyst	None	Negative
Hiddle-stone	30	M	Mid-lobe	Lobectomy	Cyst	None	Negative
Levin	38	M	R.U. lobe	Segment resected	Cyst	None	Negative
	25	M	R.U. lobe	Lobectomy	Cyst	None	Negative
Godfrey	52	M	R.U. lobe	Lobectomy	Cyst	None	Negative
Naji	64	M	R.U. lobe	Lobectomy	Cyst	None	Negative
				COMPLEX ASPERGILLOMAS			
Hemphill	58	M	R.U. lobe	Drainage	Abscess	None	Negative
Foushee	44	M	R.L. lobe	Lobectomy	Bronchiectasis	None	Negative
Bruce	52	M	L.U. lobe	Lobectomy	Bronchiectasis	None	Positive
Graves	72	M	R.U. lobe	Lobectomy	Abscess	None	Negative
				ASPERGILLAR INFECTION OF SUPPURATIVE LESIONS			
Krasnitz	29	F	L.U. lobe	Segment resected	Abscess	"Stormy"	Negative
Hiddle-stone	28	M	L.L. lobe	Lobectomy	Abscess	None	Negative

found in suppurative pulmonary lesions, but no circumscribed mass of fungus (aspergilloma) is formed (Fig. 3). The mycelium is seen, sometimes only after a careful search with special staining techniques, invading the walls or lying amid the debris within the walls of abscess cavities. The underlying disease in the 2 cases of this type in our series was pulmonary suppuration with or without bronchiectasis.

We have also encountered aspergillar infection of empyema spaces in 3 patients who had broncho-pleural fistulæ following pneumonectomy for tuberculosis, but these have not been included in this series.

C. *Allergic Aspergillosis.* The third group consisted of 3 cases of allergic aspergillosis. In all 3 resection was undertaken because the persistence of radiological shadows led to the suspicion of carcinoma. Examination of the resected lobes showed atelectasis and characteristic filling of bronchiectatic bronchi by inspissated mucus. The mycelium of the fungus was demonstrated in this mucus by silver staining (Hinson *et al.*, 1952). Subsequent study showed the characteristic features of allergic aspergillosis: pneumonia migrans, *Aspergillus fumigatus* in the sputum, and a blood count of over 1,000 eosinophil cells per cu. mm.

Material

A study has been made of 21 patients who were operated upon by the surgeons at the London Chest Hospital. Applying the definitions outlined above, they have been classified as follows: simple aspergilloma 6 cases, complex aspergilloma 10 cases, secondary fungal infection 2 cases, and allergic aspergillosis 3 cases. Some of the details of these patients are shown in Table I. Sixteen of the patients were men and the average age was 47 years. In the cases reported in the literature there was a similar predominance of males and a similar age incidence (see Table II). These published cases have been classified as far as possible in the same way as those in the series reported here, and the result of the analysis is shown in Table III.

Table III.—Synopsis of Cases

Type	*London Chest Hospital cases*	*Published cases*	*Total*
Simple aspergilloma	6	16	22
Complex aspergilloma	10	4	14
Aspergillosis in pulmonary suppuration	2	2	4
Allergic aspergillosis	3	—	3
	21	22	43

This table shows that the cases reported in the literature have mostly been examples of simple aspergilloma by our definition. We believe that complex aspergillomas are, in fact, more common than simple aspergillomas, but that the former are not often reported because the fungal element is a relatively insignificant part of the main disease, and these cases are not often subjected to the detailed histological and bacteriological study which is usually necessary to establish the diagnosis.

Results

The results of the operations in the combined series are shown in Table IV. These figures show that, whereas there were few post-operative complications amongst the patients with simple aspergillomas, and none in those with allergic aspergillosis, the incidence of complications in the group of complex aspergillomas and in those with aspergillosis in suppurative lesions was formidable.

Two patients died after operative treatment for simple aspergilloma: one of these had a bronchopleural fistula and died after a lobectomy in the early days of thoracic surgery (Deve, 1938), and the other had marsupialisation of the cavity only (Pesle and Monod, 1954). No other recorded case had any complication, but one of the 6 patients in the present series developed a broncho-pleural fistula and an empyema.

TABLE IV.—LONDON CHEST HOSPITAL AND PUBLISHED CASES COMBINED

Type	*Number*	*Morbidity*	*Mortality*
Simple aspergilloma	22	1 (5%)	2 (9%)
Complex aspergilloma	14	6 (43%)	1 (7%)
Aspergillosis in pulmonary suppuration	4	2 (50%)	1 (25%)

The results of surgery in patients with complex aspergillomas were very different; there were complications in 6 of the 10 patients in our series, and, in addition, one died after operation. In one of the 6, an air leak which developed on the tenth day closed spontaneously, but in the remaining 5 cases serious bronchopleural fistula or empyema, or both, occurred. Of the 4 cases of this type reported in the literature, none had complications.

Complications followed operation in both patients in whom diffuse aspergillar invasion of suppurative lesions had taken place. In one an air leak developed but did not lead to the formation of an empyema; the other patient had a bronchopleural fistula and died. In one of the two cases in the literature, the convalescence was described as "stormy" (Krasnitz, 1957), but in the other no complications were recorded (Hiddlestone *et al.*, 1954).

If the figures for the patients in our series with complex aspergillomas are combined with those with aspergillosis in suppurative lesions, it will be seen that post-operative complications, both fatal and non-fatal, occurred in no less than 9 out of 12 patients (75 per cent.). This includes 2 patients (17 per cent.) who died and 7 patients (58 per cent.) who had complications after operation. Two of these survivors died one and three years later of pulmonary insufficiency and are not included in the post-operative mortality figures.

EXAMINATION OF THE SPUTUM

In nearly all of our cases a thorough search had been made for the presence of aspergillus in the sputum; this is done as a routine measure in all cases with undiagnosed pulmonary lesions. The organism was isolated from the sputum before operation in 2 of the 6 patients with simple aspergillomas, in 6 of the 10 with complex aspergillomas, in one of the 2 in which there was diffuse fungal invasion of suppurative lesions, but in none of the 3 patients with allergic aspergillosis.

Overall, *Aspergillus fumigatus* was isolated from the sputum before operation in 9 of our 21 cases (Table 1). This high proportion of positive isolations is in striking contrast to the findings in the cases reported in the literature; in the 22

recorded cases the fungus was found before operation in only 2 cases, one was an example of simple aspergilloma and the other an example of complex aspergilloma (Table II). This difference emphasises the need for a thorough search for the organism in the sputum in patients with pulmonary lesions of doubtful ætiology. This is particularly important when the characteristic shadows of aspergillomas are seen in X-ray films of the chest.

In all save one of our 9 patients in whom the organism was found in the sputum, operation was followed by complications; the one exception was a case of simple aspergilloma. On the other hand, complications occurred in only 2 of the 12 patients from whose sputum no fungus was isolated. The fungus is more readily found in the sputum of patients with complex aspergillomas because the lung disease is then more extensive and the bronchi draining the cavities are bronchiectatic, whereas it is characteristic of simple aspergillomas that there is no such associated bronchiectasis.

The higher incidence of serious complications after operations on patients with complex aspergillomas, and in those in whom fungal invasion of suppurative lesions has taken place, is probably due to the widespread pulmonary disease and the severity and frequency of secondary bacterial infection. Nevertheless, the presence of the aspergillus in the sputum may be an indication of this more severe disease, and this must be taken into consideration when surgery is contemplated.

Conclusions

The surgical results show that resection of simple aspergillomas carries little risk, and, clearly, if the diagnosis is in doubt, surgery should be recommended because carcinoma is such a common cause of rounded shadows in X-ray films of the chest. If however the diagnosis is reasonably certain, as judged by the presence of *Aspergillus fumigatus* in the sputum and of the characteristic radiological picture of a crescentic air space above a solid shadow, operation may not be required. Surgical removal of a *simple aspergilloma* is justified if there is a great increase in the size of the lesion or troublesome hæmoptysis.

Complex aspergillomas present a more difficult problem. Because of the high incidence of complications following operation in these cases resection must be avoided if possible. The extensive disease often present in the rest of the lungs rather than the aspergilloma itself is the factor most likely to shorten the patient's life. On the other hand, repeated bacterial infection of the affected lobe may make surgical intervention necessary even in the face of the high rate of complications.

Surgery should be avoided in cases of *allergic aspergillosis*. In these cases a part of the lung is usually bronchiectatic and this is infected by *Aspergillus fumigatus*. The surgeon may consider resecting the bronchiectatic lobe, or a lobe which remains collapsed for many months, with the object of removing the supposed primary source of the fungal infection and so arresting the progress of the disease. Our experience has indicated two reasons why this should not be done. In three cases, including only one of the present series (the other two were lost to our follow-up), resection was followed by further pneumonic

episodes, continued blood eosinophilia and persistence of the fungus in the sputum. In other cases not operated upon, all the manifestations of allergic aspergillosis gradually died out, in the majority of cases, over periods of one to five years (Plummer, 1958).

Summary

Attention is drawn to the hazards of surgery in the presence of aspergillar infection of the lungs.

Twenty-one cases of aspergillosis, in which surgery had been carried out, are reviewed, and the results are analysed along with those in twenty-two cases from the literature.

The cases are divided into three types, aspergillomas (simple and complex), aspergillar infection of suppurative lesions, and allergic aspergillosis.

Surgery is relatively safe in patients with simple aspergillomas, but the incidence of post-operative complications in patients with complex aspergillomas combined with those who had aspergillar infection of suppurative lesions was very high (75 per cent). Two of the nine patients who had complications died after operation. The indications for surgery in such cases are discussed.

Surgery is neither necessary nor desirable for the localised lesions of allergic aspergillosis.

We are indebted to Dr. K. F. W. Hinson and his assistants at the London Chest Hospital for the pathological work on these cases of aspergillosis, and to our medical and surgical colleagues at this Hospital for permission to study their cases.

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THE PULMONARY COMPLICATIONS OF ŒSOPHAGEAL DISEASE

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Medical reporting passes through well-recognised phases. First there appears the report of the rare or unusual case. Others follow, and then the review of the collected cases previously reported, with the addition of a short series reported for the first time by the author. During the next phase in the history of any lesion it becomes recognised with increasing frequency, ceases to be a rarity and loses the appeal of novelty; little is written about the subject at this stage. Subsequently, the newcomer takes its assigned place in the catalogue of diseases, appears for the first time in the standard textbooks of medicine, and collects a few decorations in the form of complications and sequelæ, whose association with the parent condition has only recently been recognised. Finally, there appears the comprehensive survey of a record-breaking series which disposes of the problem and establishes not only the relative frequency of the condition but a true perspective against which its significance and relationship to other or associated conditions can be assessed. This stage has yet to be achieved in the subject under discussion.

Any new concept in the field of pathology or therapeutics arouses undue interest, often incommensurate with its significance. Enthusiasm in medicine and surgery can be dangerous and infectious. To maintain a sense of proportion and the faculty of purely objective observation against the background of some of the dazzling advances of recent years is not always according to our inclination. But unless this discipline is rigidly enforced the case will probably be overstated to the lasting regret of all concerned. Too much manure applied to the young plant will kill it.

The responsibility of œsophageal disease for certain cases of acute and chronic lung infection has been recognised only recently, and dates from the time when a growing acquaintance with œsophageal physiology and pathology brought to light the lack of responsibility frequently shown by the œsophageal sphincters, superior and inferior, and the fact that the laryngeal and cough reflexes are considerably depressed during normal sleep and by certain drugs. The third line of defence of the air passages, the ciliary action of the bronchial mucosa, can be overwhelmed by the sudden inhalation of any quantity of regurgitated food. The object of the present communication is to re-emphasise the relationship and its diagnostic importance against the background of a personal series of 1,308 cases of œsophageal disease investigated and treated by the author.

The problem can be approached in one of two ways. On the one hand the incidence of pulmonary complications in a series of cases investigated primarily for œsophageal disease can be ascertained and recorded. Here the symptoms

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caused by the œsophageal lesion are predominant; symptoms of complicating pulmonary disease may cause the patient little discomfort or disability and can only be brought to light on direct questioning. Occasionally the patient may volunteer a history suggesting pulmonary infection, but this is unusual as the patient himself does not appreciate the relationship and therefore assumes that his cough, expectoration and dyspnœa are not relevant to his chief complaint of dysphagia and regurgitation. On the other hand, the case may present as one of acute or chronic lung damage occurring for no apparent reason, at a time of year when chest infection is uncommon, and affecting areas of the lung fields not normally involved by the commoner infections such as bronchitis, tuberculosis or bronchiectasis. It is this aspect of the problem which is the main concern of this paper.

TABLE I.—INCIDENCE OF ŒSOPHAGEAL LESIONS IN BELCHER'S SERIES OF 48 CASES WITH PULMONARY COMPLICATIONS

	Cases
Achalasia of cardia	34
Œsophageal strictures	6
Pharyngeal diverticulæ	5
Carcinoma of œsophagus	3
Total	48

Any attempt at a statistical review of the frequency with which pulmonary damage complicates œsophageal disease is difficult for various reasons. Firstly, chronic pulmonary infection is so common that in any particular case it is often impossible to assign responsibility to any one cause. Secondly, the pulmonary complications rarely follow any definite pattern. Thirdly, although it is well recognised that major œsophageal obstruction, as in achalasia of the cardia and malignant stenosis of the œsophagus, may, and frequently does, result in lung damage due to aspiration pneumonitis, the significance and importance of gastro-œsophageal reflux due to sphincter incompetence commands less general recognition and agreement.

In 1949 Belcher reviewed 39 cases, previously reported, of pulmonary suppuration complicating œsophageal disease, and added a further 9 cases of his own. The commonest antecedent œsophageal lesions were achalasia of the cardia and pharyngeal diverticula in 34 and 5 cases respectively (Table I).

TABLE II.—INCIDENCE OF VARIOUS ŒSOPHAGEAL LESIONS IN AUTHOR'S SERIES OF CASES INVESTIGATED FOR PULMONARY COMPLICATIONS

	Cases
Hiatus hernia of diaphragm (including 142 cases of benign stricture secondary to reflux œsophagitis)	736
Primary carcinoma of œsophagus and cardia ..	412
Achalasia of cardia	71
Congenital atresia of œsophagus	65
Pharyngeal diverticulum	18
Chemical strictures of œsophagus	6
Total	1,308

In the author's cases (Table II) these lesions are relatively uncommon as compared with other œsophageal abnormalities as the potential cause of gastro-œsophageal reflux and aspiration. Hurst (1943) had recognised the significance of achalasia in the causation of lung infection and reported a series of cases with predominantly pulmonary symptoms, in whom the œsophageal lesion caused little or no disability and remained unsuspected and unrecognised until revealed by barium swallow examination.

TABLE III.—INCIDENCE OF PULMONARY COMPLICATIONS IN SERIES REVIEWED AND REPORTED BY BELCHER

	Cases
Lung abscess	18
Pulmonary fibrosis	10
Pneumonitis	8
Bronchiectasis	6
Lipoid pneumonia	4
Atelectasis	2

The pulmonary complications in Belcher's series are shown in Table III. The commonest was lung abscess. This is now a rare lesion, but the incidence of œsophageal disease remains unchanged, although the pattern of the lung complications is changing. Patchy pneumonitis and subsequent pulmonary fibrosis were considerably commoner in the author's cases than any other manifestation of pulmonary aspiration.

It is generally accepted that the reason for the association is the relaxation of the pharyngo-œsophageal sphincter mechanism during sleep, and the regurgitation of œsophageal contents retained in the organ as a result of obstruction; or, in its turn, failure of the lower sphincter, as in hiatus hernia, to restrain gastric contents from welling up into the œsophagus under the influence of the positive intra-abdominal and negative intra-thoracic pressures, assisted by changes in posture such as stooping forward or lying flat at night.

The change in the pattern of the pulmonary complications invokes other possible explanations. The most potent cause of gross pulmonary suppuration and abscess formation is probably open dental sepsis, although the rising standard of living and improved education have undoubtedly contributed to the wider use of the toothbrush and greater awareness of the dangers of oral sepsis. In the cases reviewed by Belcher dental sepsis, in addition to reflux and aspiration, may have contributed to the high incidence of abscess formation, although no specific mention was made of this factor. Recurring aspiration pneumonitis is as common as ever, but is now chemical rather than infective. The severity of the injury to the bronchial mucosa caused by the aspiration of undiluted gastric secretion has been observed previously; actual necrosis of lung tissue as a result of " acid digestion " has been reported. That the recurring aspiration of small quantities of gastric juice can give rise to a more insidious, low-grade, chronic infection, is less well recognised.

The following pulmonary lesions have been observed in the present series of 1,308 cases of œsophageal disease.

1. Lung abscess was uncommon as compared with the incidence in Belcher's

series. When present it was usually in the form of small multiple abscess cavities within an area of chronic aspiration pneumonitis, revealed only on examination of a resected lobe. Less commonly an area of aspiration pneumonitis may break down and excavate with a rapidity suggestive of actual digestion of lung tissue rather than suppuration due to infection and gangrene. When this occurs the patient may raise only small quantities of muco-purulent sputum and there is little correlation between the dramatic radiological appearances and the relative mildness of the patient's symptoms.

2. Acute, recurring and chronic aspiration pneumonitis was the commonest pulmonary complication observed. The segments of lung tissue normally affected, the axillary portions of the upper lobes and the apical segments of the lower lobes, are those most frequently involved in any aspiration phenomena (Brock, 1946). The onset was often acute and resolution characteristically slow; some evidence of residual pulmonary fibrosis or secondary bronchiectasis usually followed. Hæmoptysis in the initial stages was followed by cough, purulent expectoration, pleuritic pain and dyspnœa. The radiological appearances did not serve to differentiate the lesion from aspiration pneumonitis arising from other causes, such as chronic sinus infection or oral sepsis, but in the absence of any discernible cause it seemed justifiable to assume a direct relationship between the lung infection and the co-existing œsophageal lesion. The radiological, and in particular the tomographic, appearance of the lesion strongly suggested a bronchial carcinoma in many instances, and even exploratory thoracotomy might fail to exclude this possibility. In such a case the only way of obtaining a satisfactory biopsy specimen is by excising the whole segment or lobe for examination. Owing to the slow resolution of the lesion clinical observation might prove equally unreliable in differentiating between the two conditions.

3. Atelectasis, segmental or lobar, and uncomplicated by infection, was less commonly observed. Cases in this group were usually referred for further investigation with a provisional diagnosis of carcinoma, a diagnosis only abandoned after bronchoscopy, tomography and, in some cases, exploratory thoracotomy, had failed to confirm the presence of a tumour. Eighty per cent. of the cases of congenital atresia of the œsophagus in this series were complicated by the presence of atelectasis of the upper lobe of the right lung, resulting from aspiration of the saliva and not infrequently aggravated by the use of excessive quantities of iodised oil in diagnosis.

4. Chronic bronchitis was a common coincidental finding, but no suggestion is made that the primary cause of this complication was œsophageal reflux. Common diseases frequently co-exist in the absence of any ætiological relationship.

5. Progressive chronic diffuse pulmonary fibrosis, unassociated with observed acute attacks of lung infection, and frequently leading to complete disability from crippling dyspnœa, was observed in a few cases. The concept of "idiopathic," *i.e.* unexplained, pulmonary infection or fibrosis of unusual type is no longer generally accepted; as in other instances of "idiopathic" disease, improved methods of investigation and diagnosis have steadily reduced the

number of cases in which no simple and logical explanation is forthcoming. Many cases of diffuse and patchy pulmonary fibrosis have been studied and recorded (Baglio *et al.*, 1960) but the welter of speculation on ætiology accompanying these reports omits any consideration of œsophageal reflux and bronchial aspiration as possibly responsible for, or contributing to, the pulmonary damage; nor were any investigations carried out to eliminate this factor. The association is not sufficiently obvious to attract the notice of the physician unless his attention is focused upon the part that œsophageal disease may play in such a case.

6. Hæmoptysis, unassociated with any other pulmonary symptoms, radiological changes or bronchoscopic evidence of neoplastic disease, was the presenting symptom in an appreciable number of cases. Many similar cases investigated in the past were thought to be due to dry bronchiectasis and, when a bronchogram failed to reveal any bronchial dilatation, the failure to confirm this diagnosis was assumed to be due to imperfections in bronchographic technique. The hæmoptysis might recur from time to time but only small quantities of blood were raised. The patients stated that they felt perfectly well and volunteered no other complaints. A routine barium swallow examination, however, might, and often did, reveal the presence of an hiatus hernia of the diaphragm, complicated by gastro-œsophageal reflux and confirmed by œsophagoscopy. Direct questioning might elicit symptoms of gastro-œsophageal reflux, seldom severe enough to cause the patient any distress or inconvenience or, in the absence of œsophagitis, to justify any surgical attack on the hernia. However, in the absence of any other feasible explanation the possibility that the hæmoptysis could result from recurring episodes of nocturnal gastro-œsophageal reflux and aspiration of gastric secretion into the bronchial tree during sleep should be considered. On the other hand, the absence of any other evidence, either clinical or radiological, of chest infection or damage such as is known to follow the aspiration of gastric secretion, casts doubts on this explanation. The mode of causation of the hæmorrhage is not obvious and again the association may be fortuitous, although the relative frequency of the association suggests a causal relationship.

7. In a series of 736 personal cases of hiatus hernia of the diaphragm, in patients over the age of 10 years, some degree of bronchiectasis was encountered in approximately 5 per cent. It is tempting here also to assume a causal relationship, but there is scant justification for so doing. The bronchiectasis revealed by bronchographic studies was localised in the left lung thrice as commonly as on the right, whereas it is known that all bronchial aspiration phenomena are commoner in the right lung in the ratio of 4 or 5 to one in the left lung. In this series there was probably no direct relationship between the two conditions. From the practical point of view, however, it is in the patient's interest to establish the association of left-sided basal bronchiectasis and an hiatus hernia of the diaphragm. In the event of a resection being indicated for the bronchiectasis, the opportunity should be taken to repair the hiatus hernia at the same time, to save the patient from the necessity of a further thoracotomy at a later date, with little or no increase in the risk of the operative procedure.

To summarise, the assumption of a direct relationship between the pulmonary complication and the œsophageal cause would be justified only if the following conditions are fulfilled:

(i) Location of the lung lesion in a common " aspiration site."
(ii) Demonstration of an œsophageal lesion commonly associated with regurgitation of œsophageal contents or gastro-œsophageal reflux, *e.g.* hiatus hernia of the diaphragm, benign or malignant œsophageal strictures, achalasia, œsophageal diverticulum.
(iii) Absence of oro-nasal sepsis.
(iv) Absence of any obstructive lesion, neoplastic or inflammatory, of the bronchial tree on bronchoscopy, bronchography or tomography.
(v) Absence of any evidence to suggest other forms of trauma to the bronchial tree.

A detailed presentation of cases in which there seemed to be sufficient evidence to warrant the assumption of a direct relationship between the œsophageal disease and the pulmonary complications is in preparation. The object of this brief communication is to stimulate a line of enquiry in all cases of chest infection, acute, recurring or chronic, of obscure ætiology that will ultimately afford sufficient evidence on which to base more definite conclusions.

In the present state of our knowledge it can be stated merely that any form of œsophageal obstruction, dysfunction or reflux can give rise to recurring, sometimes devastating, pulmonary complications; that this association is probably commoner than was previously suspected. Investigation of these cases should include barium studies of the œsophagus and stomach, but equally important is an accurate history from the patient. As has been stressed already, he may not volunteer any information regarding symptoms referable to the œsophagus, as to him they appear irrelevant; only on direct questioning will the essential facts be elicited. Any history of vomiting, regurgitation, dysphagia, substernal or epigastric discomfort, acid reflux and heartburn, especially when aggravated by changes in posture such as stooping or lying down, is significant and relevant in this context. The onset of pulmonary symptoms may but not invariably coincide with an exacerbation in the œsophageal symptoms, as the reflux and aspiration which cause the more insidious damage usually occur at night during sleep. Œsophagoscopy, preferably under local anæsthesia, by an endoscopist experienced in the interpretation of minor changes in œsophageal function as well as the grosser forms of œsophageal obstruction, should be performed. Serious or progressive œsophageal diseases discovered in this way, such as benign or malignant strictures, achalasia or diverticulæ, should be treated on their merits. However, the presence of pulmonary complications, probably progressive, should undoubtedly influence the surgeon when deciding the indications for surgical treatment in any case of œsophageal disease. When the œsophageal lesion proves on investigation to be incompetence of the œsophago-gastric sphincter mechanism, with or without an hiatus hernia of the diaphragm, the indications for surgical treatment are more difficult to assess. The presence of reflux œsophagitis would in itself justify surgical repair

of the hernia, but in those more numerous cases where this complication is absent and symptoms of reflux are minimal, only the risk of permanent pulmonary damage and the absence of any other likely cause of the pulmonary infection would justify surgical treatment of an otherwise asymptomatic hernia.

Summary

1. Œsophageal and gastric disease associated with regurgitation or reflux and the potential risk of aspiration into the bronchial tree is common.

2. Severe, progressive and disabling pulmonary damage may result from this cause.

3. The possibility of an underlying and causative œsophageal lesion should be considered in every case of pulmonary inflammation of obscure ætiology and the appropriate investigations carried out as part of the routine examination of such a case.

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A CASE OF MULTIPLE PULMONARY "HAMARTOMATA" OF UNUSUAL TYPE

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The diagnostic difficulties associated with the radiographic discovery of a solitary circular shadow in the lung of a symptomless patient are too well known to require elaboration. The possibilities range from the completely benign to the violently malignant, and an immediate and conclusive answer is often only obtainable by thoracotomy.

The discovery of several round shadows involving both lungs might be regarded as narrowing the diagnostic field with a bias in favour of malignancy: benign tumours and developmental abnormalities, with the exception of arterio-venous aneurysm, are generally single (Simon, 1956). If tuberculomata and hydatid disease can be excluded the occurrence of bilateral circular opacities makes metastatic malignant deposits the first choice in differential diagnosis.

The following case is of interest not only because it proved to be an exception to the rule that benign tumours of the lung are almost invariably single, but also because of the diagnostic problem provided, which was only resolved after the most careful and detailed pathological examination.

Case Report

Mrs. A.B., æt. 50, was first seen at the Stoke-on-Trent Chest Clinic in June 1957 following a Mass Radiography examination a week previously. This had revealed circular opacities in both lung fields (Fig. 1).

Her only symptom was a morning cough accompanied by scanty mucoid sputum which she attributed, probably quite correctly, to smoking forty cigarettes daily. At first she maintained that she had always enjoyed excellent health, but in response to more detailed questioning she recalled that some twenty years previously she had attended a local hospital for a course of deep X-ray treatment for "goitre." Her symptoms at that time were tachycardia and loss of weight and her attendances at the hospital had extended over a period of four months. The hospital, although able to confirm her attendance for radiotherapy, was not in a position to supply details as the clinical records had been destroyed.

She was a healthy-looking intelligent woman in excellent general condition. Clinical examination revealed no abnormality in the respiratory or cardio-vascular systems. The thyroid appeared normal and there was no evidence of thyrotoxicosis. A Mantoux test was positive to 10 units O.T., sputum was

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culture negative for *M. tuberculosis* and the E.S.R. gave a reading of 10 mm. in the first hour. A Casoni test was negative.

Metastatic malignant disease was considered to be the most likely diagnosis, and in view of the lack of information regarding the nature of the earlier thyroid abnormality she was referred to the Christie Hospital and Holt Radium Institute in Manchester for investigation. The thyroid function was found to be normal and no radio-iodine concentration was detected in the lung lesions. Thoracotomy was advised but declined.

Throughout the following year she remained in excellent health and the X-ray appearances were unaltered. A film taken in August 1958, however, gave the impression that the opacities, particularly that in the left lung, had enlarged while the right diaphragm had risen by about one interspace, suggesting possible liver involvement (Fig. 2).

Thoracotomy was again advised and after some hesitation the patient finally agreed to enter hospital.

The pre-operative investigations added nothing to the existing information and showed no contraindication to surgery. On October 28, 1958, a right thoracotomy was carried out by Mr. J. M. Sanderson. The lower lobe of the right lung was found to contain numerous subpleural nodules of firm consistence and about 2 mm. in diameter. Two warty nodules, pink and fleshy in appearance and about 4 mm. in diameter, were removed, together with the rounded nodule shown clearly in the X-rays, which measured $2 \times 1{\cdot}5 \times 1{\cdot}5$ cm. These specimens were examined in the Pathology Department of the North Staffordshire Royal Infirmary by Dr. A. J. McCall, to whom we are indebted for the following report:

"The swellings are formed largely of interwoven smooth muscle fibres which are often very attenuated. Some collagen is present but no elastic. Spaces of varying size are present throughout the tissue and these are lined by low cuboidal epithelium which is occasionally multilayered. In many places quite well-formed papillary epithelial processes project into the cavities and in these the epithelium is taller (columnar).

"The lesions appear to be the result of a developmental abnormality. They are not ordinary leiomyomata but some kind of hamartoma."

The sections from the resected specimens were later submitted to Dr. K. F. W. Hinson, who likewise regarded them as an unusual variety of "hamartoma" with a fibroadenomatous structure instead of the chondroadenomatous tissue usually found in these lesions.

The patient made a rapid and entirely trouble-free recovery from the thoracotomy, but the large rounded shadow in the left lung was still looked upon with some misgiving, particularly in view of its increase in size during the eighteen months period of observation. It was felt that the discovery of a series of benign tumours in one lung did not wholly justify the assumption that an obvious and fairly gross abnormality in the other was equally benign, and accordingly a left thoracotomy was done on April 6, 1959, when Mr. Sanderson again found numerous small nodules scattered throughout the lung tissue. The large mass which had been radiologically evident was lying subpleurally in the fissure between the apical and lateral segments of the lower lobe and was removed. It measured $3 \times 2 \times 2{\cdot}5$ cm. and appeared as a multilocular cyst with watery contents. The fluid within the cyst was reported as showing a chemical affinity to plasma but with a low protein content. Two other nodular

masses were removed from the lingula and lower lobe respectively and all three specimens were again examined by Dr. A. J. McCall, who reported:

" The microscopic appearances in these tumours are essentially similar to those previously described. Many of the solid areas are similar in appearance to uterine leiomyoma. Many of the epithelial-lined spaces are cleft-like. Stains for mucin in the epithelium are negative, though mucin is abundant in the epithelium of a small bronchiole which is attached to the surface. Serial sections have been examined from one of these swellings, but this has shed no further light."

The patient again made a good recovery from the operation and when last seen was fit and well apart from her usual morning cough with its accompanying mucoid sputum.

Discussion

This case is reported in detail because we have been unable to find any record in the literature of an instance of multiple pulmonary lesions of similar type and also because it provides an exception to the general rule that benign tumours and developmental abnormalities in the lung occur singly. In describing it as an instance of multiple hamartomata the term " hamartoma " is being used in its broadest sense. This term was originally introduced by Albrecht (1904) when he suggested that tumours could be divided into two main categories, the choristomata which consisted of tissues not normally present in the particular organ involved, and the hamartomata which resulted from an abnormal mixture of the normal tissue elements of the organ. The abnormality in the hamartoma could be either in the quantity of the tissue, in its arrangement, in its degree of maturity, or in a combination of these faults, and the term in effect was so defined as to cover the majority of benign growths wherever they occurred.

In later reports the word hamartoma, when applied to pulmonary lesions, has been employed in a much more restricted sense and has been reserved to describe a specific tumour composed mainly of cartilage which occurs singly, seldom gives rise to symptoms and exhibits no tendency to malignant change (Carlsen and Kiaer, 1950; McDonald *et al.*, 1945; Jackson *et al.*, 1956). More recently Adams (1957) has discussed the nomenclature and has suggested the term " chondroadenoma of the lung " for these cartilaginous tumours.

The growths resected from this case clearly differ considerably from the currently accepted pattern of pulmonary hamartomata both in their histological structure and their multiplicity, and we would suggest that the term " benign pulmonary fibroadenomatosis " would probably reflect accurately the pattern and distribution of the lesions.

Summary

A case of multiple benign pulmonary tumours is described in which the histological pattern was predominantly fibroadenomatous. Nomenclature is discussed on the basis of the original definition of hamartoma and the descriptive title " benign pulmonary fibroadenomatosis " is suggested.

We are indebted to our colleagues Mr. J. M. Sanderson and Dr. A. J. McCall for their invaluable help and interest in the investigation of this case, and to Dr. K. F. W. Hinson for examining the tissue sections from the first series of specimens.

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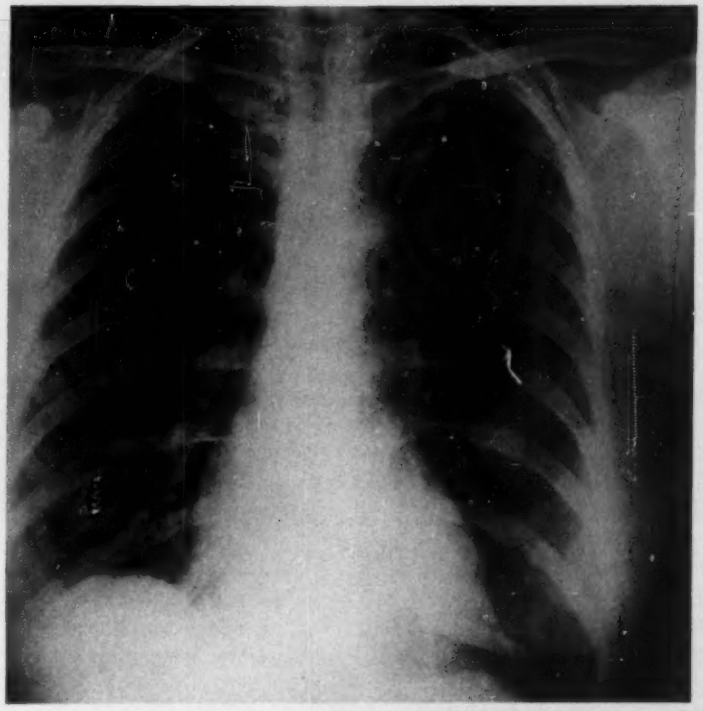

FIG. 1—Film of May 1957 showing rounded opacities in right lung at level of the tip of the fourth rib and at the fifth interspace, with a large circular shadow at the tip of the fifth rib in the left lung.

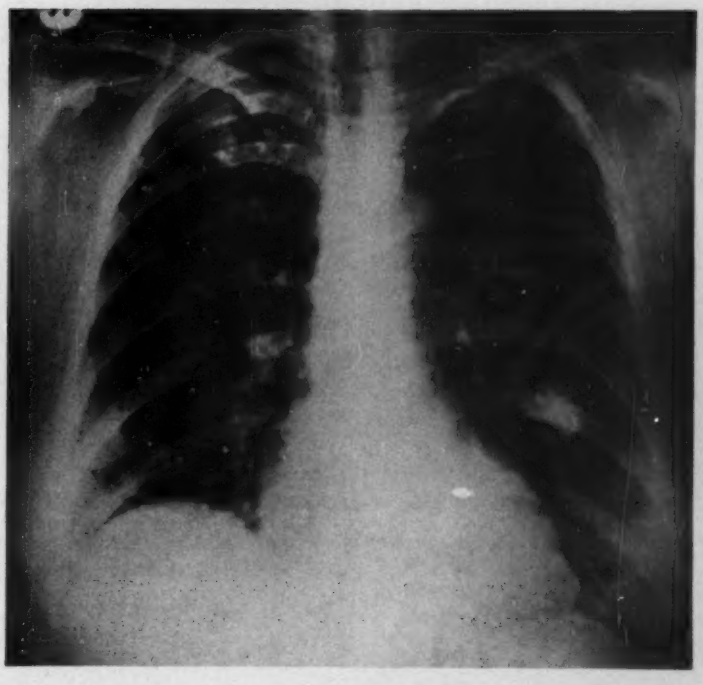

FIG. 2.—X-ray of August 1958 showing apparent enlargement of the opacities in both lungs.

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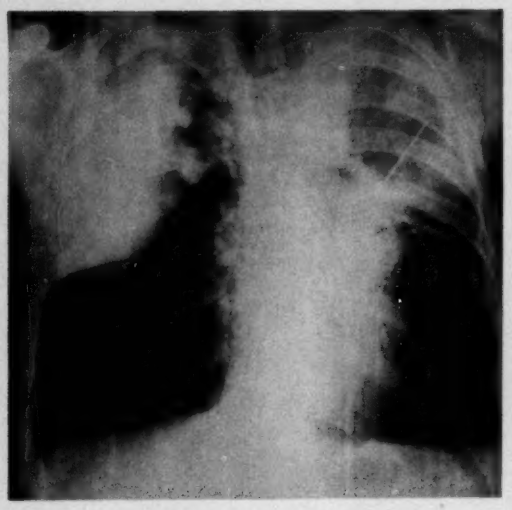

FIG. 1.—Radiograph showing needle in left pleural space.

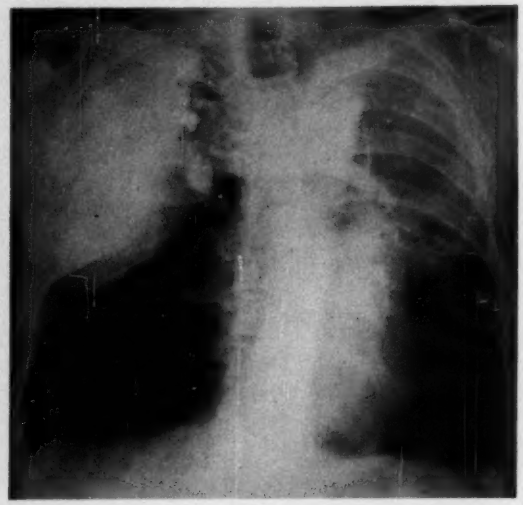

FIG. 2.—Radiograph showing needle in right pleural space.

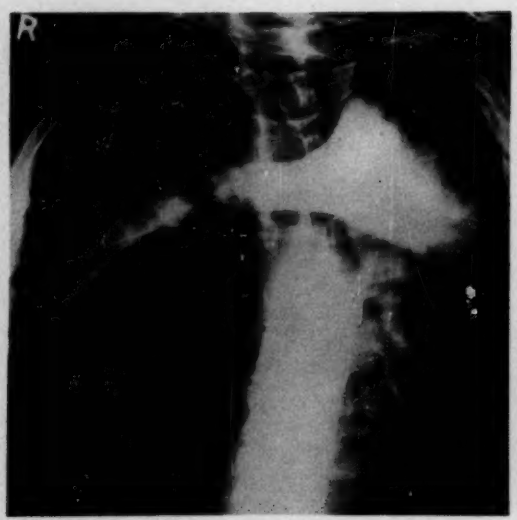

FIG. 3.—Pleurogram showing communication between pleural spaces.

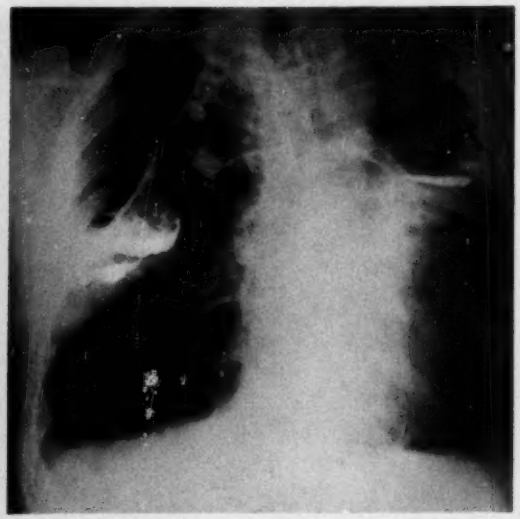

FIG. 4.—Pleurogram outlining the pleural spaces.

Brit. J. Dis. Chest (1960) **54**, 353.

ACQUIRED COMMUNICATION BETWEEN THE PLEURAL CAVITIES

REPORT OF A CASE

By E. J. M. Weaver

From the Department of Thoracic Surgery, The London Hospital

Communication between the pleural cavities is not a recognised abnormality and a search of the literature has failed to reveal a recorded case. No congenital communication between them can be envisaged, as at no stage in the process of development are they represented by a common cavity. In their definitive state they are intimately related, especially behind the upper end of the sternum, where the two parietal pleuræ are not separated by mediastinal structures. It is at that site that a rupture between the two cavities could take place, causing a possible complication of fracture of the sternum. It may be an explanation of the bilateral pneumothoraces which are sometimes seen in that condition, when the clinical evidence suggests that only one lung has been injured. An example of this has been seen by the author, in which a left intercostal tube controlled both pneumothoraces. That type of communication is only transitory, as are the ones which result from intrathoracic surgery, but the permanent one recorded below appears to be sufficiently unusual to warrant publication.

Case Report

History.—A man, aged 52, had been receiving treatment for pulmonary tuberculosis for twenty-six years. In 1932 a left artificial pneumothorax had been induced and four years later a right one was also instituted to control his bilateral disease. Both of them were maintained until 1946, when they were allowed to obliterate with fluid formation; re-expansion of the left lung was more complete than the right. No further treatment was given until 1951 when, owing to breathlessness, monthly right pleural aspirations were begun at a chest clinic. In 1954, while an aspiration was being performed, the needle broke in the right pleural cavity. At that time it was decided that no attempt should be made to remove it, but that the patient should attend regularly to assess his progress. A chest radiograph taken in 1955 (Fig. 1) showed that the needle was now lying in the left hemithorax, but one taken a month later revealed that it had returned to the right pleural cavity (Fig. 2). It was as a result of this strange occurrence that the patient was referred to Mr. Vernon Thompson at the London Hospital.

On Investigation.—The sputum and right pleural fluid were negative for A.F.B. on smear and culture. Following aspiration of the right pleural effusion Neohydriol was injected into the space. The pleurograms obtained demonstrated a communication between the pleural cavities (Figs. 3 and 4).

At Operation (Mr. V. C. Thompson).—On March 12, 1956, a right thoracoscopy was performed and the needle, which was lying free in the pleural space, was removed. The communication leading to the left pleural space was

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seen to be a circular opening about 2 cm. in diameter, situated in the superior mediastinum lying immediately posterior to the upper end of the sternum.

Comment

The occurrence of a defect similar to the one recorded above must be extremely rare, and the means of its production are not obvious. The patient was originally treated by a left artificial pneumothorax and the radiographs taken at that time show no migration of air into the right pleural cavity. It seems probable that the parietal pleuræ remained intact for the ten-year period during which the bilateral pneumothoraces were maintained, as a connection between them would have been noticed when refills were being performed.

Assuming that the communication developed after the pneumothoraces were abandoned, three possible causes are suggested: (1) An empyema burst from one pleural cavity into the other. (2) The needle, which broke in the right pleural cavity, punctured the mediastinal pleuræ. (3) The mediastinal parietal pleuræ ruptured as a result of a pressure differential between the two cavities.

1. *Bursting of an Empyema.*—This is extremely unlikely as there was no clinical evidence that the patient had ever had an empyema. Pus was not obtained from the right pleural cavity and frequent cultures of the aspirate from 1951 onwards were sterile.

2. *Needle Puncture.*—A radiograph taken after the aspirations had begun in 1951, but before the needle broke in 1954, showed an opacity across the superior mediastinum outlining the communication similar to that seen in Fig. 2. In view of this the needle could not have been responsible.

3. *Development of a Pressure Differential.*—Owing to the poor expansion of the right lung after the pneumothoraces were abandoned a higher negative pressure may have been present in the right pleural cavity as compared with the left. The right pleural aspirations may have aggravated this, with the result that the parietal pleuræ ruptured at the site of immediate contact; namely, behind the upper end of the sternum where the communication was located.

I wish to express my thanks to Mr. Vernon Thompson for his advice and permission to publish this case.

Brit. J. Dis. Chest (1960) **54**, 355.

FIBRINOID NECROSIS IN THE BRANCHES OF THE PULMONARY ARTERY IN CHRONIC NON-SPECIFIC LUNG DISEASE

By M. S. Dunnill

From the Department of Pathology, The Radcliffe Infirmary, Oxford

In recent years there have been numerous reports of fibrinoid necrosis and arteritis affecting the branches of the pulmonary artery in primary pulmonary hypertension and in pulmonary hypertension complicating congenital or acquired heart disease. The following case is of interest because of similar lesions which were present in a case of right heart failure complicating chronic bronchitis and emphysema.

Case Report

The patient was a retired lorry driver, aged 58 years at the time of his death. He had suffered from a chronic cough with production of mucoid sputum all his life, and for the past fifteen years had been increasingly breathless on exertion. In 1952 he had an attack of right-sided lower lobar pneumonia and after this his symptoms became more severe. In May 1959 his breathlessness became extreme and he could only walk 100 yards with difficulty. He was admitted to hospital with early congestive failure, dyspnœa and cyanosis at rest. Examination of the chest revealed a severe degree of emphysema. The sputum contained numerous pus cells and *Strep. viridans* and *Str. pneumoniæ* were grown on culture. No tubercle bacilli were isolated. He was treated with antibiotics and digitalis without much improvement as he remained somewhat cyanosed at rest. He was discharged home at his own request and remained at home until December 1959, when he was readmitted to hospital with severe congestive cardiac failure and died the day after admission.

Post-mortem Findings (PM. 968/59)

Necropsy was performed 24 hours after death. The body was that of a well-built male with ankle and sacral œdema. There was mild clubbing of the fingers and toes.

The *heart* (650 g.) showed striking right-sided dilatation and hypertrophy; the right ventricle measured 1·2 cm. in thickness at its base. The left ventricle measured 1·6 cm. in thickness. There was no evidence of congenital, rheumatic or ischæmic heart disease. The main pulmonary artery was dilated and flecked with atheroma.

The lungs were fixed by intrabronchial perfusion with 10 per cent. formol saline and four days later were cut into slices 1 cm. thick. There were small areas of saccular bronchiectasis present in the anterior segments of the upper lobe and in the lateral segments of the middle lobe of the *right lung*. Throughout the rest of this lung there was fairly extensive emphysema which was mainly of the centrilobular variety. In the upper lobe there were scattered areas of more irregular emphysema surrounding several small focal areas of fibrosis. The *left*

(*Received for publication July* 15, 1960.)

lung showed a small area of saccular bronchiectasis in the lingula of the upper lobe. Scattered areas of focal fibrosis were present in the lower lobe and both lobes showed a severe degree of centrilobular emphysema. The normal bronchi in both lungs contained mucopurulent plugs, but there was no gross evidence of pneumonic consolidation in either lung. The walls of the small branches of the *pulmonary artery* appeared thickened throughout both lungs.

The *liver, spleen and kidneys* showed chronic passive venous congestion only and the other organs were unremarkable.

Histology

The findings of interest were confined to the lungs. The *large bronchi* contained pus and mucus. The bronchial mucosa showed a variety of changes consisting of extensive goblet cell hyperplasia, areas of ulceration and areas where the normal respiratory mucosa had been replaced by simple stratified epithelium. Submucosal vasodilatation and chronic inflammatory cell infiltration were prominent features. The *smaller bronchi*, *bronchioles* and *terminal bronchioles* frequently contained mucopus. Areas of focal dilatation were common and mural infiltration with lymphocytes, plasma cells and neutrophil polymorphonuclear leucocytes, with destruction of smooth muscle, was frequent. The *lung parenchyma* showed well-marked areas of centrilobular emphysema together with several areas of focal fibrosis. There was no actual pneumonia, the inflammatory changes being mainly in the bronchioles.

Sections of the *main pulmonary trunk* showed atheroma. The elastic configuration in the media was of the normal adult type. The *elastic or conducting pulmonary* arteries, vessels measuring 1 mm. or more in diameter, showed focal areas of intimal fibrosis with some lipoid deposition. The *muscular pulmonary arteries*, vessels measuring between 1 mm. and 0·1 mm. in diameter, showed changes of a most dramatic nature. These vessels were often situated at the centre of a cluster of emphysematous spaces (Fig. 1). In many instances the media was replaced by an irregular mass of fibrinoid material (Fig. 2) which showed clearly in hæmatoxylin and eosin preparations, but was even more obvious in sections stained with Masson's trichrome or phosphotungstic acid hæmatoxylin. There was interruption of the internal elastic lamina in the affected vessels. In addition those muscular pulmonary arteries which were not the seat of fibrinoid necrosis often had a somewhat fibrosed media, with a replacement of muscle by fibrous tissue, and orcein preparations showed interruption of the internal elastic lamina (Fig. 3). This finding suggested that these vessels represented healed fibrinoid necrosis. A cellular reaction to the fibrinoid necrosis of the type found in polyarteritis nodosa was not present, but in a few arteries there were small focal collections of lymphocytes in the adventitia. The arterial lesions were distributed evenly over both lungs and the upper and lower lobes were equally affected. The *pulmonary arterioles*, vessels of less than 0·1 mm. diameter, showed some intimal fibrosis, but no evidence of fibrinoid necrosis or arteritis. The *bronchial arteries* in the areas of bronchiectasis were slightly dilated, but were not otherwise remarkable.

Discussion

Patients with the clinical diagnosis of chronic bronchitis and emphysema usually show numerous pathological changes in the lung with localised areas of

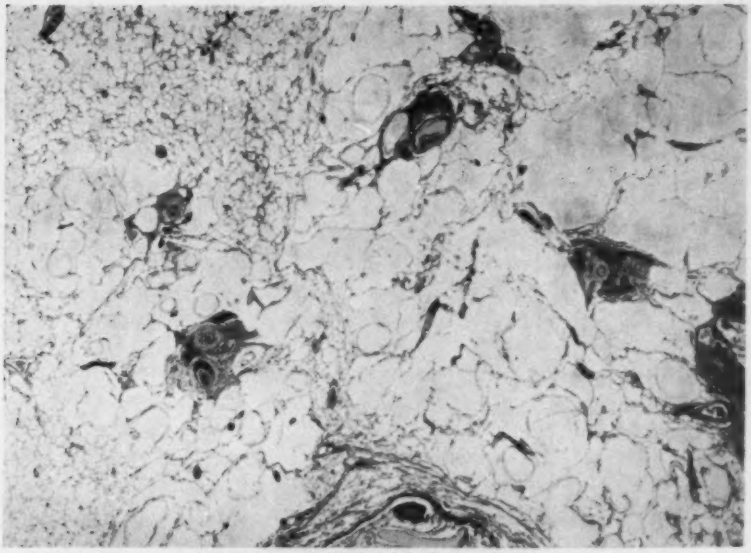

FIG. 1.—Lung showing centrilobular emphysema. The branches of the pulmonary artery, which have been filled with an injection mass, can be seen to be greatly thickened. Hæmatoxylin and eosin. (×5.)

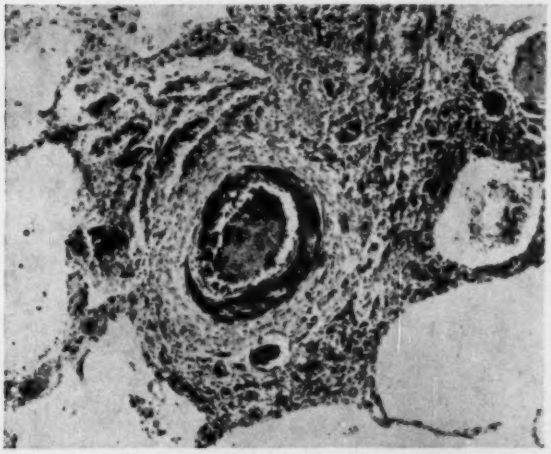

FIG. 2.—A muscular pulmonary artery, in the centre of a cluster of emphysematous spaces, showing fibrinoid necrosis in the media. Masson's trichrome. (×20.)

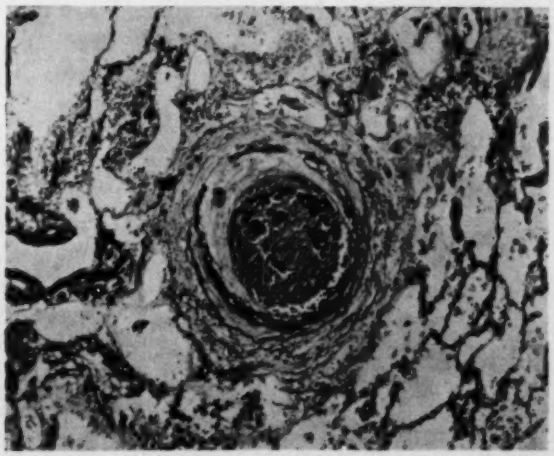

FIG. 3.—A muscular pulmonary artery showing intimal fibrosis. There is interruption of both internal and external elastic laminæ possibly representing a healed fibrinoid lesion. Orcein. (×20.)

To face p. 396

bronchiectasis, chronic inflammatory changes in the other bronchi, focal areas of fibrosis in the lung parenchyma and various forms of emphysema. It is for this reason that it is more logical to refer to these cases as suffering from chronic non-specific lung disease. The occurrence of right ventricular hypertrophy and congestive cardiac failure in such cases is well known, but the vascular lesions seen in the lungs are usually unconvincing. Medial hypertrophy is seldom present (Heath and Best, 1958), though Harrison (1958) claims that it may sometimes be seen in the small muscular pulmonary arteries. Intimal fibrosis in the arterioles is the most frequent finding, but as McKeown (1952) points out the significance of this is difficult to assess as it sometimes occurs with advancing age. In cases with bronchiectasis, Liebow, Hales and Lindskog (1949) have demonstrated the presence of precapillary broncho-pulmonary arterial anastomoses in the diseased regions, but Spain (1959) asserts that unless the bronchiectasis is extensive these are not important in raising the pulmonary artery pressure and causing right ventricular hypertrophy. In this case the bronchiectasis was not widespread. Destruction of the pulmonary capillary bed by the emphysematous process is seldom extensive enough to cause pulmonary hypertension, as it has been shown experimentally that at least 70 per cent. of the lung must be destroyed before this occurs (Flores, Adams and Perkins, 1954). Probably the most important cause of pulmonary hypertension in these cases is the anoxia which occurs during attacks of acute pulmonary infection (Whittaker, 1954). When the infection is controlled, and the anoxia relieved, the pulmonary artery pressure falls, though it may not reach normal levels. Heath and Best (1958) suggest that it is because the pulmonary hypertension is not sustained that medial hypertrophy is not seen in the muscular pulmonary arteries.

The pathogenesis of fibrinoid necrosis of arterial vessels in both systemic and pulmonary hypertension is still a matter of debate. Pickering (1955) has suggested that it may depend on the rate at which the pressure rises as well as the actual level of the pressure. In cases of cor pulmonale the pulmonary pressure is seldom as high as in cases of congenital or rheumatic heart disease with pulmonary hypertension. In the case described here it is probable that the chronic bronchial and bronchiolar infection, with consequent anoxia, was never adequately controlled after his first admission to hospital. The anoxia and raised pulmonary artery pressure were thus maintained for an unusually long period, some six months, and this was probably the most important factor in the causation of the arterial lesions.

Summary

A case is described of a man with chronic bronchitis and emphysema dying of right heart failure. The muscular pulmonary arteries showed a striking degree of fibrinoid necrosis.

I am grateful to Sir George Pickering and Dr. A. H. T. Robb-Smith for their helpful advice in preparing this paper.

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REVIEWS OF BOOKS

Die Asbestose der Lungen. By Dr.Med. H. Bohlig, Dr.Med. G. Jacob, Dr.Med. H. Muller. Stuttgart: Georg Thieme Verlag. Pp. 166. DM. 59.40

This monograph deals with pulmonary asbestosis and provides a comprehensive review of the whole problem.

In the introductory chapters the history of asbestos mining, the various methods of industrial usage of asbestos and the methods of prevention of asbestos dust are described.

Subsequently the pathological anatomy of asbestosis and its pathogenesis are extensively discussed, with a detailed description of some experimental work.

The main part of the book deals with the clinical problems of asbestosis and the complications of the disease, with an analysis of the incidence of lung cancer and a brief mention of therapy.

Finally, there is an excellent, well illustrated account of the radiological manifestations of asbestosis. The problems of radiological differential diagnosis and complications which were manifested on routine radiological examination are clearly brought out.

The section on lung function studies is very short; this is unfortunate since the book loses thereby some of its value. The bibliography covers the world literature and is completely up to date.

As a monograph this is a most useful volume, since it covers a wide field and brings together much data from many sources.

R. E. Steiner.

Roentgenology of the Chest. Edited by Coleman B. Rabin. Springfield, Illinois: Charles C Thomas. 1958. Pp. 484. Illus. £7 7s.

Fifty authors, physicians, surgeons and radiologists have collaborated in this book to "present roentgenology of the chest to the roentgenologist from the clinical standpoint and to the clinicians from the radiological point of view."

There are 464 pages of text with numerous illustrations, followed by a comprehensive index. The first 353 pages are devoted to radiological techniques and the normal radiological anatomy, followed by descriptions of the various pathological processes involving the thoracic cage, the pleura, diaphragm, mediastinum and lungs. This wide field has been well covered, but the authors have been limited by the space available to the basic and more common manifestations of disease. There are several very interesting chapters in this section, such as "The influence of intra-alveolar pressure upon the roentgen appearances of the chest." "Some special signs in chest roentgenology" and "Diffuse interstitial pulmonary fibrosis." The pulmonary mycoses are described in some detail, with the accent on North American experience of these conditions.

An attempt has been made to cover the radiological investigations and the diseases of the heart and great vessels. Whilst there are several good chapters in the section, it has not been possible to provide in a mere 110 pages more than an introduction to this subject.

In both the pulmonary and cardiac sections there are frequent references to the value of fluoroscopy and, indeed, several authors appear to regard this as a routine examination. Dotter, alone, points out the great limitations of this method. It is unfortunate that many clinicians and even some radiologists still disregard or are unaware of the fact that fluoroscopy provides a high radiation dose. The skin dose produced by one minute of fluoroscopy approximates to that from 100 P.A. chest films. In this reviewer's opinion fluoroscopy should only be used to obtain specific information that is not already available from a study of the clinical findings and radiographs.

This book has been attractively presented by the publishers. There is a wide divergence in the style of writing, inevitable in a book of this type, but the majority of chapters are well written and well illustrated. All but a few are followed by an adequate list of references as a guide to further reading.

This book will be welcomed by students as an introduction to the radiology of the chest.

J. N. PATTINSON.

The Treatment of Bronchial Neoplasms. By ROBERT R. SHAW, M.D., and DONALD L. PAULSON, M.D. With a chapter on "Bronchial Adenoma" by JOHN LESTER KEE Jr., M.D. Springfield, Illinois: Charles C Thomas. 1959. Pp. 135. Illus. £3 4s.

To all those responsible for the treatment of patients suffering from bronchial carcinoma this monograph will be of particular interest in its critical approach to the choice of current therapeutic methods for the individual case. It is an account of the authors' experiences of 1,180 cases of bronchial carcinoma and 35 cases of bronchial adenoma under their personal care between 1945 and 1957. Early enthusiasm for total pneumonectomy for bronchial carcinoma has been curbed in the light of experience, and a strong plea is made for lobectomy when feasible, on the grounds of lower mortality and lessened morbidity. Full use is made of sleeve resections and various bronchoplastic procedures to preserve lung tissue, and stress is laid on the pathological type of growth as the main factor influencing survival time, and hence the choice of treatment. Resectability rate was 35 per cent., 50 per cent. being judged inoperable at the first visit and a further 15 per cent. inoperable at thoracotomy. Immediate and long-term results are compared, and compare very favourably, with those reported from other major surgical centres. Operative mortality was 9 per cent. for pneumonectomy and 3 per cent. for lobectomy. Both radiotherapy and chemotherapy are discussed and find an important place in relieving symptoms, but are shown to have little effect on survival time although three patients have survived more than five years.

Bronchial adenoma comprises 3 per cent. of the series and the clinical features are contrasted with those of bronchial carcinoma. The majority had symptoms of bronchial obstruction and pulmonary suppuration with or without hæmoptysis. The tumour was visible bronchoscopically in 80 per cent. Surgical excision with maximum conservation of healthy lung is the treatment of choice. Bronchoplastic procedures have a special place in treatment and were possible in five cases with excellent results.

F. H. SCADDING.

Diagnosis and Treatment of Diseases of the Trachea and Bronchi. By HERMAN J. MOERSCH and HOWARD A. ANDERSON. Springfield, Illinois: Charles C Thomas. 1960. Pp. 105. Illus.

We have grown to expect a high standard from the staff of the Mayo Clinic and this small book is no exception. Each chapter is short, concise and without irrelevant material.

The theory is advanced that in chronic bronchitis the mechanical irritation of coughing is capable of perpetuating the condition, and it is likened to sandpaper rubbing up and down inflamed air passages. If this is correct, all expectorants are contra-indicated (if any are effective in any case). The authors, at the same time, condemn antitussive drugs except for short-term use for sleeping or breaking the habit of coughing.

The Mayo Clinic figures for carcinoma of the lung show that in males squamous carcinoma is much greater than adenocarcinoma, presumably because the former has a closer relationship to smoking. Scalene biopsy, thoracentesis, needle biopsy and thoracotomy may be necessary when other diagnostic procedures fail. The figures quoted for diagnosis by cytological examination of the sputum are better than most centres can achieve.

The book contains chapters on rarer conditions, such as tracheoectasis, alveolar cell tumour and tracheal carcinoma. Fairly dogmatic criteria are enumerated for and against bronchoscopy in pulmonary tuberculosis. Plastic surgical procedures for stenosis when this condition is quiescent, and for carcinoma of the trachea, are considered. Broncho-stenosis may be masked by asthmatic presentation, which responds well to bronchoscopic dilatation. The pendulum seems to be swinging back towards surgery for bronchiectasis, despite antibiotics and physiotherapeutic posturing.

The lack of an index is justified by the book's small size. All the X-rays are exceptionally clearly reproduced and in spite of a few minor examples of carelessness the book can be thoroughly recommended.

LESLIE G. ANDREWS.

A Textbook of Medicine. Editors RUSSELL L. CECIL, M.D., Sc.D., Emeritus Professor of Clinical Medicine, Cornell University; and ROBERT F. LOEB, M.D., Sc.D., D.Hon.Causa., LL.D., Bard Professor of Medicine, Columbia University. Philadelphia and London: W. B. Saunders. 1959. Pp. 1665. 115s. 6d.

Since it first appeared in 1927 Cecil's textbook of medicine has been deservedly popular among students and physicians in the English-speaking world. The tenth edition will enhance its high reputation and recruit a host of new readers, for it is doubtful whether so much up-to-date knowledge can be found elsewhere in such readable and balanced form or in such reasonable compass. As in previous editions there are a large number of contributors, and among them all the great names in North American medicine as well as two from England and one from Canada. Despite this multiple authorship—the contributors number over 150—there is remarkably little overlap and on this the editors are to be particularly congratulated. The references that are included after each subject are carefully and wisely chosen and give a clear guide as to where to find more detailed information should the reader desire it. The pace of progress in medicine is now so rapid and the time required to

produce and print a book of these dimensions is so considerable that it is inevitable that the most recent advances in knowledge cannot be included. Such omissions are, however, few, and it is to be hoped that subsequent editions will appear at shorter intervals than three or four years as has been the practice in the past, otherwise some sections are bound to become seriously out of date. There is little to criticise, but not many physicians would agree that sympathectomy still holds an important place in the treatment of hypertension or that radiotherapy is of value in peptic ulceration. The use of oral diuretics in the treatment of heart failure receives too scant attention, and there are the usual errors that have escaped the proof-reader's eye, such as the indexing of multiple myeloma. Nevertheless it is the best textbook of medicine available to-day and the tenth edition will be welcomed and acclaimed by clinicians everywhere.

A. G. W. WHITFIELD.

Die Tuberculose, Ihre Erkennung und Behandlung. By H. DEIST and H. KRAUSS. Stuttgart: Ferdinand Enke Verlag. Pp. 847. DM.138.

This book gives a comprehensive survey of the diagnosis and treatment of all forms of tuberculosis as practised in Germany. There are chapters on the pathology, bacteriology and immunology of tuberculosis. Public health problems and measures of control of this disease, pulmonary, genito-urinary and bone and joint tuberculosis are all adequately dealt with, while other chapters are devoted to tuberculosis of the skin, eye and ear.

Yet there is much dead wood which could be left out with advantage. Thus the lengthy discussion on sanatorium treatment and the indications for and against artificial pneumothorax seem out of date. Altogether the treatment of the various forms of this disease differs throughout from present-day Anglo-American trends in thought and practice. The methods of administration of the anti-tuberculous drugs, for instance, seem still to be in a state of flux. Thus, one much favoured regimen gives the drugs in the following manner: Streptomycin 1 g. three times a week, 10 days of INAH 400 mg. daily, followed by 5 days of Thiosemicarbazone 0·05 g. t.d.s., which is then followed again by 10 days of INAH, and so on. Streptomycin is given, on the average, only to a total dosage of 20-25 g. Thiosemicarbazone is still much favoured, while the use of the more recent drugs, *e.g.* Viomycin, Cycloserine and Pyrazinamide, are only fleetingly mentioned. The surgical treatment of pulmonary tuberculosis also differs from Anglo-American practice. For instance, extra-pleural pneumothorax and even oleothorax are preferred on the whole to thoracoplasty. While the indications for lung resection are the same as in this country, the importance of adequate pre- and post-operative chemotherapy is not stressed and may, therefore, account for the high fistula rate and post-operative spread mentioned. A very conservative attitude, based on morbidity and mortality figures of the pre-chemotherapy era, is taken in the treatment of tuberculosis of the female tract. Radiotherapy is accordingly given in preference to surgical treatment, while on the other hand the duration of chemotherapy (twelve months) recommended is short by modern standards.

The book is well produced and gives an insight into the present position of tuberculosis and its treatment in Germany.

H. C. NOHL.

L'Expertise de la Silicose Pulmonaire (*Bilan du Collège Regional de Nancy*). PAUL SADOUL and MAURICE DUSAPAIN. Masson et Cie. 1959. Pp. 234. 42 illustrations. Fr.2,400.

It was Sterne who said long ago that " they order these things better in France." Today, in methods of compensation for pneumoconiosis, France compares more than favourably with other countries. In their recent monograph entitled " L'Expertise de la Silicose Pulmonaire " Professor Sadoul and Dr. Dusapain describe these methods in detail. The most notable arrangement is that in certain difficult and contested cases claimants for compensation are examined by a board (known as a College) of three physicians with wide experience in occupational chest diseases. Colleges have been set up at Clermont-Ferrand, Limoges, Lyon, Montpellier, Nancy, Nantes, Paris, Toulouse and Lille. In this book the authors describe the activities of the Nancy College from 1954 to 1957, during which period they dealt with 1,240 patients, of whom 55 per cent. were coal miners, 16 per cent. iron miners, 6·8 per cent. granite and sandstone workers, 6·3 per cent. foundry workers, 2·9 per cent. refractory workers, 2 per cent. slate quarry workers and 11 per cent. from miscellaneous industries including tunnelling and potteries. All these patients came from a large industrial area in the North-West region of France.

At first, only patients with right heart and pulmonary complications such as tuberculosis and pneumothorax were seen by the College, but since October 1957 three other groups of cases have been submitted: those in which the period of exposure to dust seemed too short for the onset of pneumoconiosis; when the employers, unions or the State contested the primary diagnosis made by a single expert; or in cases in which more than five years had elapsed between the termination of exposure to dust and the making of a claim for compensation.

The outstanding feature of the work of the Colleges is the thoroughness of the investigations carried out before a decision is reached. Each claimant is admitted to hospital for five or six days, and undergoes clinical examination, X-ray examination which includes fluoroscopy, two standard X-ray films, and in more than one-third of the cases, tomography. In addition, electrocardiographs are taken and the patients are submitted to extensive lung function tests. Measurements of respiratory variables during exercise of constant intensity and of alveolar gas exchanges are often made. The sputum is, of course, examined for tubercle bacilli and blood sedimentation rates are determined as a routine measure. In some cases, with the consent of the worker, right heart catheterisation is done to determine the presence or absence of pulmonary hypertension.

At Nancy the College has the advantage of using the facilities of Professor Sadoul's first-class and progressive physiological laboratory, and it is undoubtedly true that, while a diagnosis of pneumoconiosis can be made by clinical, X-ray and occupational studies, the assessment of disability must be made by estimation of the pulmonary and cardiac function.

I had the privilege of assisting at one of the sessions of the Nancy College, and I can testify to the meticulous care by which a decision is reached in each case. To paraphrase Lord Hewart, justice was not only done, but was manifestly seen to be done.

The book is strongly recommended to all who are interested in diseases of the chest.

A. I. G. MCLAUGHLIN.

Le Cathéterisme du Cœur Droit et des Artères Pulmonaires en Pneumologie. By P. TROCME and J. CHEDAL. Masson et Cie. 1958. Pp. 110. Illustrated. Fr.1,600.

After a preliminary, somewhat sketchy, account of the technique of cardiac catheterisation, the authors proceed to describe the results obtained in a variety of chest diseases, adding in most cases some results of their own. They also describe the technique of selective angiography of segments, lobes and lungs. They feel that these methods will not only yield much of academic importance, but are also most valuable clinically to physicians and to surgeons. They emphasise that clinical and electrocardiographic methods are most inaccurate in the detection of *cor pulmonale*, in particular in its incipient stage. Thus, for example, they recommend catheterisation of the chronic bronchitic, so that if he is found to have a raised pulmonary arterial pressure he may be given extra prophylactic care, particularly during acute exacerbations. This surely reflects an extraordinary state of affairs; it is inconceivable that in this country anyone could seriously advance such a view; and it is to be hoped that this is the case in France also, where, after all, an ancient tradition of clinical wisdom cannot be displaced entirely by an ultra-scientific approach, by which some younger French investigators are trying to make up for the sterility of the war years and the preceding decades. These remarks are not to detract from the value of the work as a whole, which gives a good survey of the field, and a good bibliography. Like all such works it is unfortunately already out of date in part. Unilateral and lobar emphysema and vascular anomalies are not discussed, and amongst the pharmacological studies the value of acetylcholine in the elucidation of the nature of pulmonary hypertension, as shown by Paul Wood, is not mentioned.

Tuberculose Pulmonaire. Roles des Ganglions Lymphatiques. Ph. SCHWARTZ. Masson et Cie. 1959. Pp. 228. Fr.3,000.

In this volume the author returns once more to the subject of so many of his previous publications—the role of the lymphatic glands in the "bronchogenic spread of pulmonary tuberculosis." He demonstrates by means of careful dissection, photography and radiographs that not only in childhood tuberculosis is hilar adenopathy important, but in adult tuberculosis also the majority of the lesions are caused by rupture of caseous lymph nodes or even peribronchial lymph follicles into the bronchial pathways, with consequent aspiration into the pulmonary parenchyma. He does not ignore the hæmatogenous factor, but proposes to deal with this aspect in a subsequent book. Much of the material was collected when Schwartz was working in Istanbul, but he forestalls the suggestion that the observations are only applicable to non-Europeans by asserting that his findings are no different from those made in Germany and in the U.S.A. Turkey simply provides a multitude of autopsies by reason of a higher incidence of the disease.

Schwartz's ideas on pathogenesis are very much at variance with those accepted by most authorities in explanation of the majority of the phenomena of adult tuberculosis. Clinically also, careful observation does not often yield evidence of bronchial perforation by lymph glands, even when it is suspected. Nevertheless, the meticulous dissections of Dr. Schwartz are very convincing, and his ideas have attracted a large number of authorities, particularly in France. With these facts in mind, his book should be most interesting and stimulating to all working in the field of tuberculosis. The French is simple, the production excellent, and the photographs are clear and well labelled. L. J. GRANT.

BOOKS RECEIVED

The following books have been received and reviews of some of them will appear in subsequent issues.

Quarterly Progress Report of the Veterans Administration—Armed Forces Study on the Chemotherapy of Tuberculosis. Washington, D.C.: Veterans Administration Department of Medicine and Surgery. April 1960.

Newer Virus Diseases. Clinical Differentiation of Acute Respiratory Infections. By John M. Adams. The Macmillan Co. of New York. Pp. 292. Price 40s.

L'Hippocratisme Digital, l'Ostéo-Arthropathie Hypertrophiante et les autres dysacromélies apparentées. By Charles Coury, Professeur Agrége à la Faculté de Medicine, Paris. Paris: J.-B. Baillière et Fils. Pp. 230.

Missbildunger des Menschlichen Herzens. Priv. Doz. Dr. Heinz Barthel, Prof.Dr. W. Doerr and Prof.Dr. R. Nissen. Stuttgart: Georg Thieme. Pp. 237. Illus. Price DM. 188.

Radiologische Exploration des Bronchus. Prof.Dr. S. Dirienzo and Dr. H. H. Weber, Stuttgart: Georg Thieme. Pp. 281. Illus. Price DM. 54.

REPORTS

FUTURE OF CHEST SERVICE

THE dramatic decline in the incidence of tuberculosis in all but the oldest age groups during the past few years is reflected in a report on the future of the chest services prepared by the Standing Tuberculosis Advisory Committee.

One of the main recommendations is that in new hospitals beds should be available for diseases of the chest, some of them being set aside for cases of tuberculosis. Similar provision should be made in existing general hospitals where possible; otherwise existing suitable Sanatoria and chest hospitals could be used as chest departments of nearby hospitals or run in close association with them.

After recommending that the chest physician should be a member of the staff of a general hospital, with a primary duty to tuberculosis patients, the report emphasises that it is important that he should work closely with the Medical Officer of Health on epidemiological and preventive implications, and continues: "The end of the epidemic prevalence of tuberculosis in our community can now be seen as an attainable object, although it may be many years ahead.

"The normal pattern of the future should be that appointments in chest diseases should be to the staffs of general hospitals, the chest clinic being integrated into the general out-patient department of the hospital and sharing the general services of the department."

DEATHS FROM TUBERCULOSIS AND CANCER, 1959*

PROVISIONAL numbers of deaths and death rates from tuberculosis and cancer in England and Wales in 1959 are announced by the Registrar-General.

Continued Fall in Tuberculosis Deaths

The total number of deaths from respiratory tuberculosis in 1959 was 3,475 (against 3,999 in 1959), giving a provisional death rate of 77 per million persons. This is a decrease of just over 13 per cent. compared with the previous year, and means that since 1949 the death rate from respiratory tuberculosis has fallen by over 80 per cent.

The death rate from other forms of tuberculosis was 8 per million persons (in 1957 and 1958 it was 12 and 11).

Deaths from Cancer of Lung again increase

The provisional death rate for all forms of cancer for men was 2,261 per million population for deaths assigned to cancer of the lung and bronchus, and a decrease from 1,549 to 1,430 for other forms of cancer. The rate for cancer of the lung and bronchus for women increased from 119 per million in 1958 to 123 in 1959 and increased for other forms of cancer from 1,810 in 1958 to 1,940 in 1959.

THIRTEENTH WORLD HEALTH ASSEMBLY, MAY 1960

AT the thirteenth World Health Assembly held on May 9 and 10, the tendency to consider the improvement of living conditions, housing, nutrition and social, as well as economic environment in general, as the main task in fighting and eradicating tuberculosis was disputed. It was held that tuberculosis must be considered primarily as an infectious disease which can occur in epidemic form under the best economic conditions as well as the worst.

Means of prevention are better than ever, but increasingly rapid international transport intensifies the danger of infection, even in countries with the highest standards of public health. There is, therefore, no room for complacency in the field of tuberculosis even in highly developed countries, and nobody is safe from tuberculosis until everbody is safe.

* The Registrar-General's Weekly Return No. 13, 1960, H.M.S.O., price 1s. 6d. net (or by post from P.O. Box 569, London, S.E.1, price 1s. 8d.)

To last four page of text

THE ECONOMICS OF SIDE EFFECTS

In tuberculosis therapy, use of the usual PAS compounds—the free acid or its sodium salt—very frequently leads to side effects or unwelcome reactions that jeopardize the overall aim of therapy . . . the patient's rapid return to normal living. Of considerable and often overlooked importance—particularly to the TB hospital and its staff—is the effect that such undesirable patient reactions to PAS administration have on the total cost of treatment:

UNDESIRABLE REACTIONS (PASA & NaPAS)	ECONOMIC RAMIFICATION
Anorexia, nausea, vomiting (present in approximately half of patients)[1]	1. *Cost of prepared but untouched or wasted meals.* 2. *Extra physician or nursing time to cope with intolerance problem.* 3. *Patient resistance leading to wastage of medication.*
Toxicity, sensitization or complete intolerance	1. *More prolonged hospital stay.* 2. *Overall cost of special care by physician, nurse and pharmacist—desensitization, dosage adjustment, etc.*
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1. Molthan, L., Cohen, R. V., and Zarafonetis, C. J. D.: Am. Rev. Tuber. 71: 220, 1955.
2. Cohen, R. V., Molthan, L., and Zarafonetis, C. J. D.: Dis. Chest 30: 418, 1956.
3. Marmion, T.: British J. Dis. Chest 53: 409, 1959.

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